

CLINICAL PAEDIATRICS

HISTORY TAKING AND CASE DISCUSSION

Third Edition

ARUCHAMY LAKSHMANASWAMY

Wolters Kluwer Health | Lippincott Williams & Wilkins

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Preface to the Third Edition

It gives me immense pleasure to come out with the third edition of *Clinical Paediatrics: History Taking and Case Discussion*. The first edition of the book was published in 2004 and the second in 2007. This edition is based on the feedback received from students, academics and clinicians on the previous two editions.

Like the previous editions, this edition also explains the clinical aspects of paediatrics in a simple manner so that it becomes easy to understand by the students. The book contains a number of mnemonics which will enable easy registration and recall of the clinical aspects of paediatrics. Further, this edition presents not only the relevant recent advances, but also several new clinical photographs, illustrations and flowcharts. All these will help students to understand the clinical problems in a better manner.

It is important for clinicians to know the normal milestones applicable to children so that any deviation from the normal can be identified and the cause can be treated. Hence, the developmental milestones are discussed in detail in this edition.

Important aspects of nutrition including breastfeeding and infant feeding are also duly emphasised in the chapter on nutrition

The common neurological disorders in children and the relevant clinical approaches are discussed in detail in the chapter on the nervous system.

The cardiovascular system as well as the gastrointestinal, renal and haematological disorders are also discussed in detail. The clinical aspects of rickets and the approach to a child with rickets have also been highlighted.

While the book is primarily designed for undergraduate students, I hope that clinicians and postgraduates also find it useful.

Suggestions for further improvement of the book would be welcomed and gratefully acknowledged.

Aruchamy Lakshmanaswamy
Salem

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I would also like to thank Wolters Kluwer who came forward to publish the third edition of this book and helped me in enhancing and updating the manuscript for this edition.

I would particularly like to thank Mrs. Sangeetha P. (Commissioning Editor) and Mr. Rajiv Banerji (Publishing Director) from Wolters Kluwer for their help and encouragement.

I would like to specially acknowledge and appreciate the constructive inputs from the editorial group at Wolters Kluwer comprising Dr. Vandana Mittal (Development Editor), Dr. Sonu Singh (former Commissioning Editor) and Dr. Arundhati Kar (former Development Editor). The inputs from all these editors have enormously helped me to improve the presentation and coverage of the book in this edition.

I would like to thank Ms. Pooja Chauhan (Production Editor) for her meticulous and painstaking help in finalising the layout and presentation for this edition as well as the other members of the Production team at Wolters Kluwer for giving the final shape to this edition.

Aruchamy Lakshmanaswamy

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CHAPTER 1

Approach to Children

A paediatrician deals with health issues in children of various age groups. During their growing years, children undergo rapid changes in their growth and development. Additionally, the clinical presentation of the same condition may be different at various ages. For example, newborn babies with infections may present with hypothermia or fever, whereas older children usually present only with fever. Hence, an approach with an open and informed mind is of utmost importance in the clinical evaluation of a child.

Even as the children enter adolescence, they feel more comfortable with the paediatrician who has been taking care of them for 12 years rather than with a new physician. Hence, it is better that medical care should be provided by the paediatrician during the sensitive adolescent period.

Children younger than 1 year feel more at ease with their mother. Therefore, it is better to examine these children while they are sitting or lying down comfortably in their mothers' lap. Older children, for example prepubertal age group, respond better when treated as independent individuals. In such children, a simple explanation of the examination or procedure before it is done yields better results.

It is also important to obtain consent from the parents (as well as the child if he or she is old enough to understand) before examination. During the examination of a female child, it is prudent to have a female attendant or female nurse in the same room.

Clinical evaluation of any disease or condition includes history taking, physical examination and summarisation of the relevant findings.

HISTORY TAKING

History taking is the foundation on which the diagnosis of any clinical condition rests. A skilfully elicited history leads to an accurate provisional diagnosis, thus reducing the range of investigations. Avoiding unnecessary investigations saves a considerable amount of time and money. The history is usually taken in the following order:

1. Name of the patient
2. Age of the patient
3. Gender of the patient
4. Place—this includes the area of current residence and the area from which they have recently migrated (if applicable)
5. Informant—mother/father/any other
6. Reliability of the informant—good/fair/not reliable
7. Presenting complaints—complaints as told by the informant/patient
8. History of present illness
9. History of past illness including the treatment history
10. History of contact with a known communicable disease (e.g., tuberculosis)

11. Antenatal history
12. Birth history
13. Neonatal history
14. Developmental history
15. Nutritional history
16. Immunisation history
17. Personal history—this is relevant if the child is above 7 years of age. This includes school performance, dietary habits and relationship with other children
18. History of allergy—skin, nasal, respiratory and gastrointestinal allergies, including allergy to food or drugs
19. Family history
20. Social and environmental history

PHYSICAL EXAMINATION

The history taking is followed by a detailed head-to-foot physical examination of the child. Components of the physical examination are as follows:

1. General examination
   - Level of consciousness
   - Nutritional status
   - Posture or attitude
   - Dysmorphic features
   - Signs of respiratory distress
   - Anaemia
   - Cyanosis
   - Jaundice
   - Clubbing
   - Significant lymphadenopathy
2. Vital signs
   - Pulse
   - Respiratory rate
   - Blood pressure
   - Temperature
3. Anthropometry
   - Weight
   - Height
   - Head circumference
   - Midarm circumference
4. Systemic examination—the system suspected to be affected should be examined first. For example, if the child presents with palpitations and cyanosis, the cardiovascular system should be examined first, followed by examination of other systems. Systemic examination includes examination of the following:
   - Cardiovascular system
   - Respiratory system
   - Gastrointestinal system
   - Central nervous system
   - Genitourinary system
   - Musculoskeletal system
   - Lymphoreticular system

Head-to-foot examination should be done for patients with diseases such as chromosomal disorders and protein energy malnutrition.

Following features should be carefully checked in children, as they may be associated with other conditions such as congenital heart defects, neurological defects, delayed milestones, and so on:

- Features of Down's syndrome
- Features of infective endocarditis
- Features of hypothyroidism
- Features of nutritional disorders/vitamin deficiencies
- Skin and hair changes related to protein energy malnutrition
- Neurocutaneous markers

SUMMARY OF THE CASE

The case summary includes relevant positive and negative findings elicited from history and examination. It can help the clinician to arrive at a definitive diagnosis and plan further management. The summary of a case should cover the following aspects:

- Provisional diagnosis
- Differential diagnosis
- Investigations
- Diagnosis
- Treatment
- Prognosis
- Prevention

CHAPTER 2

History Taking in Children

History taking is an art that requires the clinician to listen effectively to the complaints of the patients. It usually begins by asking for the basic information regarding the patient's medical history.

NAME

Documentation of the patient's name is mandatory for the identification of the patient. In addition, addressing the patient by name increases the confidence of the patient or attendant and the examiner. The name may also indicate the religion of the patient without directly asking for it. This is relevant in history taking because food practices, customs and hence certain diseases vary between different religions. For example, infection due to *Taenia solium* (neurocysticercosis) is more common in communities that eat pork and *Taenia saginata* in those that eat beef.

AGE

Age of the patient is important, as certain diseases are more prevalent in children of a specific age group. Thus, the age of the patient can be a clue to the diagnosis of the disorder. For example, rheumatic fever is more common in the age group of 5–15 years. Thalassaemia usually presents in the late infancy due to the compensating effect of foetal haemoglobin in early infancy. Vitamin deficiencies are more common in children aged 5 years or younger, as the vitamin requirement is more during this period of rapid growth. Protein energy malnutrition is seen in children aged 6 months to 5 years. Below 6 months of age, nutritional deficiency presents as failure to thrive.

Most of the congenital heart diseases usually have a younger age of onset, although the age of presentation may vary. Ventricular septal defect (VSD) usually manifests after 4–6 weeks of life, as the pulmonary pressure falls. Atrial sepal defect (ASD), on the other hand, usually manifests in the adulthood, although it is a congenital heart disease. Some heart conditions leading to cyanosis presenting at birth (5 *T*s) are *T*ricuspid atresia, *T*ransposition of great vessels, *T*otal anomalous pulmonary venous drainage, *T*runcus arteriosus and *T*etralogy of Fallot (severe pulmonary infundibular stenosis).

SEX

Many disorders, whether genetic or acquired, follow a gender bias (Table 2.1). For example, ASD and primary pulmonary hypertension are more common in females than in males. The female child is also more likely to suffer from protein energy malnutrition and child abuse. This is due to preferential nurturing of the male child in some segments of the society. Rickets, a nutritional deficiency caused by underexposure to sunlight, is also found more commonly in girls.

TABLE 2.1 Disorders with Gender Bias

Gender	Diseases
Genetic disorders	
Male	Klinefelter's syndrome Fragile X syndrome Duchenne muscular dystrophy Colour blindness Hunter's syndrome Fabry's disease Glucose-6-phosphate dehydrogenase deficiency Haemophilia
Female	Turner's syndrome Rett syndrome Rheumatic chorea
Other disorders	
Male	Cleft lip
Female	Cleft palate Anencephaly Spina bifida Patent ductus arteriosus (PDA) Congenital dislocation of hip

This is because girls spend less time outdoors and wear dresses that cover more of the body surface as compared to boys.

Genetic disorders linked to the X chromosome such as Duchenne muscular dystrophy, colour blindness and haemophilia are mostly found in males. However, these disorders may rarely be seen in females. The occurrence of X-linked genetic disorders in females can be explained by the following possibilities:

1. Lyon hypothesis—one X chromosome becomes inactive.
2. Turner's syndrome—one X chromosome is absent (XO chromosomal pattern).

PLACE OF RESIDENCE

The place of residence may give a clue about the disorder because certain diseases are endemic to certain regions. For example, endemic goitre is common in hilly regions, patent ductus arteriosus is common at high altitudes and sickle cell anaemia is common in hilly areas and tribal communities.

While documenting the place of residence, the clinician should enquire about the place at which the patient is currently residing as well as the patient's place of origin. This is relevant because disorders in these patients may match those from their places of origin rather than those from their current residential areas. People residing in or passing through the areas with endemic malaria or filariasis are more likely to suffer from it. Lead poisoning is common in children residing in places near automobile industries. To prevent this, the use of unleaded fuels is now being promoted.

INFORMANT

The informant is the person who presents the history on behalf of the child. It may be the mother, the father, the grandparents or any other person. The best person to give the history is the mother of the child. If the child is old enough to give the history, it should be recorded as well.

The documentation of the informant helps to avoid inconsistencies in the history in follow-up visits.

RELIABILITY OF THE INFORMANT

The reliability of the informant dictates the importance to be given to it. The history obtained from relatives such as uncles or aunts, who have not been very close to the child, is usually less reliable. If the informant is not reliable, then the examiner should spend more time in cross-checking the history of the child.

For example, when the informant is unsure of the date of birth, the clinician should ask questions to link it to any important event during that period. The informant may be able to say that the child was born 2 months after Diwali or in the year when a famous movie was released. If the informant is unsure about the birth weight of the child, the clinician can ask if the baby was too small or too large as compared to its siblings or other children born in the neighbourhood.

The examiner should also note the informant's intellectual level, awareness of the problem and emotional reaction to the disease. For instance, a highly emotional mother may exaggerate the events in the child's medical history.

PRESENTING COMPLAINTS

Presenting complaints include the chief complaints as told by the informant or patient. These should be recorded in chronological order of their appearance.

Example of presenting complaints

- Fever—9 days
- Cough—7 days
- Difficulty in breathing—5 days

The complaints should be recorded in the informant's or the patient's own words. The examiner should refrain from asking leading questions at this stage. Any diagnosis that is reported by the parents or derived from the opinion of other medical professionals should not be relied upon to avoid undue bias. For example, if the parent comes with the complaint 'my child is suffering from typhoid fever for past 15 days', the examiner should record it as 'fever for 15 days'.

HISTORY OF PRESENT ILLNESS

History of present illness gives a detailed account of the onset, progression and duration of various complaints in order of their appearance (see Table 2.2). Leading questions can be asked at this stage to elicit more details about the illness. The examiner may also ask appropriate questions to segregate the relevant positive history from the negative history of the illness. Medical terminologies such as oliguria and dyspnoea can be used to describe the history of presenting illness.

It is better for the examiner to start asking questions from the time when the child was normal and enquire about how the first symptom of illness appeared. Then the examiner should proceed in an orderly fashion to elicit a detailed symptom-wise (Tables 2.3 and 2.4) and system-wise (Table 2.5) history. If the child has never been normal from birth, the examiner should start from the perinatal events and neonatal history. The details of the illness and the associated factors that could have precipitated or relieved the present problems should be enquired.

If the child is already admitted as an in-patient, history of present illness should include the course during the hospital stay. If the child has been seen by various practitioners, it should be specifically mentioned and the treatment that the child has received from them must be noted.

TABLE 2.2 Components of History of Present Illness

Component	Example
Time of onset	Early morning drowsiness or convulsion is common in glycogen storage diseases. Paroxysmal nocturnal dyspnoea occurs in the night few hours after going to bed.
Mode of onset	Acute—embolic manifestations, wet beriberi. Subacute—endocarditis, dry beriberi. Insidious—nephrotic syndrome. Chronic diseases (tuberculosis).
Progression/course of illness	Condition becomes better (thromboembolic manifestations). Condition becomes worse (degenerative disorders). Static condition (cerebral palsy).
Duration of the illness	Enteric fever lasts for more than a week. Diarrhoea due to rotavirus is of short duration. Diarrhoea in inflammatory bowel diseases lasts for long duration.
Precipitating factors	Chest pain due to cardiac failure is aggravated by exertion. Chest pain due to pleuritis is aggravated by respiratory movements.
Relieving factors	Abdominal pain due to duodenal ulcer/gastritis is relieved by bland diet or antacids. Chest pain due to cardiac failure decreases with bed rest.

TABLE 2.3 Symptom-Wise Review of History of Present Illness: Fever

Attributes	Types	Possible Cause(s)
Duration	Short	Viral fever
	Long	Tuberculosis Granulomatous diseases Chronic malaria Typhoid
Rise of fever	Abrupt	Malaria Urinary tract infections Pneumonia
	Gradual	Typhoid
Course of fever	Continuous fever (temperature does not fluctuate more than 1°C throughout the day and remains consistently above the normal range)	Viral fever
	Intermittent fever (temperature fluctuation is more than 1°C and fever is present only for few hours in a day)	Malarial fever Filarial fever
	Remittent fever (temperature fluctuation is more than 2°C throughout the day and remains consistently above the normal range)	Enteric fever
	Saddle back fever (alternating febrile and afebrile periods of 2–3 days each)	Dengue fever
	Pel–Ebstein fever (alternating febrile and afebrile periods of 3–10 days each)	Hodgkin's lymphoma
	Undulant fever (fever rises and falls like a wave)	Brucellosis
	Tertian fever (fever relapses every third day)	Malaria due to *P. vivax*
	Quartan fever (fever relapses every fourth day)	Malaria due to *P. malariae*
Associated symptoms	Fever with rigors	Malaria Filaria Urinary tract infections Follicular tonsillitis
	Fever with altered sensorium	Meningitis
	Fever with convulsions	Central nervous system infection
Type of remission	Abrupt remission	Malaria (with the lysis of RBCs)
	Remission like a wave	Brucellosis

TABLE 2.4 Symptom-Wise Review of History of Present Illness: Pain

Attributes	Leading Questions and Methods to Elicit Details
Site of pain	Note whether the patient indicates the pain at a particular site with a finger or over an area with a hand.
Radiation of pain	Ask whether the pain is located at the same site or spreads to other parts of the body. Ask if the spread is gradual, acute or shooting in nature.
Severity of pain	If the child is old enough to understand, ask him/her to show the severity of pain by extending the arms (small distance for less pain and widely extended arms for severe pain). In a younger child, note whether the child is restless or crying incessantly.
Course and development	Enquire about the time of onset of the pain, its duration and whether it has improved or deteriorated.
Character of pain	Ask if the pain is stabbing, burning, colicky (waxing and waning), pricking or gnawing.
Aggravating and relieving factors	Enquire if any factors precipitate or increase the pain. Also ask about factors (including drugs) that relieve the pain, e.g., pain due to cardiac causes gets aggravated by exertion and relieved by rest. In muscular dystrophies, children complain of muscular pain that gets better with rest.

TABLE 2.5 System-Wise Review of History of Present Illness

System	Symptoms
Cardiovascular system (CVS)	
General symptoms	Dyspnoea on exertion/rest Chest pain Palpitation Cough Oedema Oliguria Haemoptysis
Symptoms specific to rheumatic fever	Fever Pain due to arthralgia/arthritis Abnormal movements (e.g., chorea) Features of cardiac failure, such as dyspnoea on exertion/rest, oliguria, pedal oedema, etc.
Symptoms specific to cyanotic heart disease	Cyanosis Cyanotic spells (Tet spells)—cyanosis occurs in Tetralogy of Fallot due to infundibular spasm Squatting
Respiratory system	
Symptoms	Cough Breathlessness Haemoptysis Wheezing Chest pain Grunting
Gastrointestinal tract (GIT) system	
Symptoms of upper GIT disorders	Pain Loss of appetite (decreased desire to eat food) Vomiting Dysphagia Melaena
Symptoms of lower GIT disorders	Diarrhoea Constipation Haematochezia (passage of frank blood in the stools) Pain
Symptoms of liver disorders	Jaundice Pruritis (itching) Clay-coloured stools High-coloured urine

(Table continued)

TABLE 2.5 *(Continued)*

System	Symptoms
Central nervous system (CNS)	
Symptoms	Altered sensorium Convulsions Visual disturbances Paralysis Focal neurological deficits
Genitourinary system	
Symptoms	Oliguria Burning micturition Haematuria Facial puffiness
Haematological system	
Symptoms	Recurrent infections (due to leucopenia)

HISTORY OF PAST ILLNESS

History of past illness includes episodes of similar or related illnesses in the past. If any such history is present, the examiner should enquire in detail about the onset of illness, treatment received (if any), course of the disease, number of episodes and frequency of relapses. Any other significant illness in the past should also be documented along with its duration, treatment and response to the treatment. History of past infections such as malaria, diarrhoea, worm infestations, respiratory tract infections, ear discharge, allergies and UTIs should be asked, especially in the case of a malnourished child. Any previous history of vaccine-preventable diseases such as tuberculosis, measles, mumps, tetanus, chicken pox, diphtheria and whooping cough should also be noted.

The examiner can ask leading questions to elicit more details and use medical terminologies to describe the history of past illnesses as well. Table 2.6 outlines some common findings in the history of past illness in a system-wise manner.

Treatment history is taken as follows:

- Prior hospitalisation (for a similar or other illness)
- Nature of treatment given (e.g., antitubercular medication)

TABLE 2.6 History of Past Illness

System	History of Past Illness
Cardiovascular system	Rheumatic fever Cyanotic spells
Gastrointestinal tract	Jaundice Blood transfusions/injections (risk of infective hepatitis) Hepatotoxic drugs Recurrent abdominal colic Chronic diarrhoea Passing worms
Central nervous system	Convulsions Exanthematous fevers Vaccinations Ear discharge

- Improvement/deterioration with the treatment
- Previous hospital stay with duration
- Irradiation
- Surgery
- Blood transfusions (indications, amount, frequency and any complications)
- Drug allergy

HISTORY OF CONTACT

The examiner may use leading questions to enquire about recent occurrence of any communicable disease in the family or in a close contact. For instance, the examiner can ask whether anybody in the family has chronic cough with expectoration to elicit history of contact with tuberculosis. Indirect evidence about this may also be obtained by enquiring if anybody in the family has been on antitubercular medication. The communicable status of the disease may be derived from the compliance to treatment and the duration of treatment completed.

History of contact with tuberculosis is present if any person in contact with the patient is a case of open tuberculosis, is on treatment with antitubercular drugs or has completed treatment within 2 years.

ANTENATAL HISTORY

Antenatal history includes the series of events that have occurred during the intrauterine developmental period of the child and may have led to the present illness. This is especially important for children with congenital defects or disorders.

An antenatal case should get herself registered in the hospital before 12 weeks of the last menstrual period and should be examined regularly. If this is not done, the patient is said to be unbooked. If the mother is a booked case, the records can be verified for the presence of maternal diabetes or infections in the antenatal period.

The clinician should enquire systematically and ask appropriate leading questions to discover all the possible antenatal offending stimuli. The offending stimulus may be a maternal disease or disorder (Table 2.7), lifestyle or habit (Table 2.8) or medication taken (Table 2.9) during pregnancy.

Important components of antenatal history are as follows:

- Age of the mother
- Weight and height of the mother
- Immunisation status of the mother (e.g., tetanus toxoid and rubella)
- Gravida
- Parity with number of children alive
- History of abortions/stillbirths
- Interval between successive pregnancies and the outcome of each (for small-for-gestational age babies)
- History of multiple pregnancies
- History of complications, such as oligohydramnios/polyhydramnios
- History of Rh isoimmunisation
- Diet during pregnancy
- History of any disease during pregnancy
- History of any infection during pregnancy, for example, HIV, intrauterine infections (TORCH) and UTIs. Rubella presents as a painful swelling behind the ears due to painful postauricular lymphadenopathy

TABLE 2.7 Effect of Maternal Disease or Disorder on Pregnancy and Infant

Maternal Conditions	Effect on Pregnancy	Effect on Infant
Diabetes	Foetal death due to acute placental failure Increased risk of preeclampsia and polyhydramnios in mother Preterm delivery	Congenital malformations (CNS, CVS and skeletal system) Birth injuries due to macrosomia Hypoglycaemia, hypocalcaemia and polycythaemia in child Hyperviscosity leading to renal vein thrombosis in child Caudal regression syndrome Respiratory distress syndrome Small left colon syndrome
Pregnancy-induced hypertension	Premature delivery Uteroplacental insufficiency Abruptio placenta Foetal loss Chronic foetal hypoxia	Growth retardation and thrombocytopenia
Systemic lupus erythematosus	Heart block and spontaneous abortions	Intrauterine growth retardation Heart block Thrombocytopenia Lupus syndrome
Congenital spherocytosis	Not significant	50% chance of inheritance
UTIs	Preterm delivery	Preterm
Hyperparathyroidism	Increased foetal loss	Tetany
Phenylketonuria	Not significant	Mental retardation Microcephaly Congenital heart defects

TABLE 2.8 Effect of Maternal Lifestyle or Habits on Pregnancy and Child

Maternal Habits	Effect on Pregnancy and Child
Direct smoking	Increased risk of placenta praevia and abruptio placenta Increased risk of stillbirth Low-birth-weight babies Mental and physical retardation in child Learning disorders and hyperactivity in child Increased incidence of cleft lip and palate
Passive smoking	Low-birth-weight babies
Alcohol	Foetal alcohol syndrome Intrauterine and postnatal growth retardation Microcephaly Characteristic facies Mental subnormality Cardiac and skeletal abnormalities
Heroin	Irritability and hyperactivity in child
Exposure to irradiation (permissible limit 500 millirads throughout the entire pregnancy period)	Abortion (more than 10,000 millirads of exposure) Microcephaly Mental retardation Cataract

- History of drug intake with dosage and duration details
- Symptoms of maternal malnutrition and vitamin deficiency

Sample leading questions to detect antenatal nutritional disorders

- What is the educational status of the mother and the father?
- What are their occupations?
- Was the mother benefited by any national programmes?
- Was she undergoing regular and timely antenatal check-up?
- What was the weight gain during pregnancy? (Normal weight gain should be 10 kg)
- Was she working during the period?
- Was she supplemented with iron and folic acid tablets? (At least 100 tablets are usually given)

Consumption of alcohol by the father may also result in foetal alcohol syndrome. Certain drugs such as lead and herbicides may affect the father's sperm. The effect of the offending stimulus on the developing child depends on which trimester of pregnancy it occurs in.

First Trimester

In the first trimester, the fertilised ovum develops into an embryo and the cells differentiate into various organ systems. During this period, there is a rapid multiplication of the cells. Any insult to the growing embryo at this stage can affect its entire development or an important organ system. Potential offending stimuli in the first trimester include viral infections, radiation, drugs and anoxia. For example, maternal rubella infection in the first trimester can lead to congenital heart diseases such as PDA or VSD in the child.

Second Trimester

By the second trimester, the embryo develops into a foetus. During this period, there is an increase in the number of cells and the size of the organs. Any

TABLE 2.9 Effect of Teratogenic Drugs, Taken During Pregnancy, on Child

Teratogenic Drug	Effect on Foetus/Newborn
Atropine	Tachycardia
Barbiturates	Depression
Beta-blockers	Growth retardation Hypotension Hypoglycaemia
Diazepam	Hypotonia Respiratory depression
Androgens	Virilisation of female foetus
Oxytocin	Placental insufficiency in large dosage Hyperbilirubinaemia (especially in girls)
ACE inhibitors	Oligohydramnios Renal dysplasia Pulmonary hypoplasia
Methotrexate	Cranial malformations Digital malformations and absent digits
Phenobarbitone	Dysmorphic facies (midfacial hypoplasia) Hypocalcaemia Coagulation defects
Phenytoin	Embryopathy/fetopathy (dysmorphic facies, microcephaly, etc.) Motor delay Mental retardation
Sodium valproate	Neural tube defects Spinal dysraphism (meningomyelocele and spina bifida) Facial dysmorphism Learning disability Motor incoordination
Carbamazepine	Neural tube defects
Trimethadione	Growth retardation Dysmorphic facies (synophrys, epicanthus and low set ears) Cleft lip and palate
Warfarin	Embryopathy/fetopathy CNS anomalies
Lithium	Ebstein anomaly Hypotonia Limb anomalies
Mercury (from contaminated fish)	Minamata disease in mother Microcephaly and cerebral palsy in newborn

insult to the foetus at this period leads to disorders of foetal organs.

Third Trimester

During the third trimester, there is rapid weight gain and increase in the size of the cells and organs that have already been formed. An insult at this stage affects the growth and functional maturity of the foetus.

Trimester	Cell number/size
First	Increase in the number of cells
Second	Increase in the number and size of cells
Third	Increase in the size of cells

BIRTH HISTORY

The birth history covers the series of events that occurred during the birth of the child. These events may have affected the child adversely and led to the present illness. The mother may be unaware of certain aspects of the birth history, especially if she was not fully conscious. The examiner can enquire about those from other members of the family present during the birth of the child or from hospital records.

Important aspects of the birth history include the following:

- Birth order: The baby born after two or three live children is prone to develop malnutrition, especially if the duration between the deliveries is less than 2 years.
- Multiple pregnancy: The second twin is at a high risk of hypoxia, hypoglycaemia and birth trauma, all of which could result in brain damage.
- Mode of delivery: Natural birth/caesarean section.
- Place of delivery: Hospital/home/any other.
- Person who conducted the delivery—qualified doctor or nurse/trained dai/untrained person.
- Gestational age: Preterm/term/post-term (prematurity predisposes the child to certain disorders such as PDA).
- Birth weight: Appropriate/small/large for gestational age.
- Birth asphyxia: Cried/did not cry soon after birth; if not, then details of resuscitation.
- Bluish discolouration of the body (e.g., on crying/feeding).
- Breathing difficulties.
- APGAR score at 1, 5 and 10 minutes after birth.

NEONATAL HISTORY

Neonatal history includes the events from birth of the baby to 28 days of its life, which are as follows:

- Feeding problems and duration of feeding
- Neonatal convulsions
- Respiratory distress syndrome
- Jaundice
- Weight gain of the baby
- History of hospitalisation, with duration and nature of treatment
- Any congenital malformations noted in this period (e.g., arteriovenous malformations)

DEVELOPMENTAL HISTORY

Developmental history includes the details of various milestones attained by the baby as it grows. This may vary from child to child. Any gross deviation is significant and should be noted.

The examiner should enquire about the various age-specific milestones. These should be compared with the normal values to detect any obvious delay in the attainment of these milestones. History of any regression in milestones should also be noted.

NUTRITIONAL HISTORY

Nutritional history includes the details of the food intake of the child right from the birth to the present eating habits. The examiner should enquire about the breastfeeding, additional diet during weaning and the postweaning diet (Table 2.10). Special focus should be given to the diet immediately before the illness.

Diet immediately before and during the illness

- Enquire about the details of food taken in the 24-hour period immediately before the present illness started.
- Calculate the calorie and protein intake of the pre-illness diet.
- Record the diet before and during the hospitalisation (especially important for diarrhoeal diseases).
- Enquire if the child was a beneficiary of noon meal scheme.

Also calculate the expected calories and protein that should be taken by the child. Now compare the present calorie and protein intake immediately prior to illness with the expected intake. An example of recording such information—the child is taking 560 cal and 12 g of protein as against expected intake of 1000 cal and 25 g of protein.

IMMUNISATION HISTORY

The disease-fighting capability of the child depends on his immune status. Therefore, it is important to enquire whether the child has been immunised or not. The examiner should also note the immunisation details (dosage and timing) of the child.

The Government of India started the Expanded Programme on Immunization in January 1978 to reduce the incidence of common infectious diseases such as diphtheria, tetanus, pertussis, polio, tuberculosis and typhoid fever. The target populations were children under 5 years of age and pregnant women. In 1985, Universal Immunization Programme was introduced in India. The target populations were the children under 1 year of age. The vaccines recommended were BCG, DPT, OPV and measles.

TABLE 2.10 Nutritional History Since Birth

Period	Leading Questions
Prelacteal feeding details	What was the time interval between birth and the first feed? What did the first feed consist of? Was colostrum fed or not? Were any prelacteal feeds such as sugar water given before breastfeeding?
Details of breastfeeding/top feeding	When was the breastfeeding started? How long was it continued? Was exclusive breastfeeding given for first 6 months or not? (Exclusive breastfeeding means feeding the baby with breast milk only; even water is not given.) If the child was partially or totally top fed, ask the following: • Which milk was used—cow's milk, formula feed or any other? • How much would the baby accept? • Was it diluted or not? If diluted, what was its dilution? • How was it given (bottle/paladai)? • Was the bottle/paladai sterilised properly?
Details of complementary feeding	When was complementary feeding (weaning) started? What was the type of the food used for complementary feeding (rice water/dal water/vegetable soups)? What were the amount and frequency of complementary food used? (The details of the quantity and quality of the food taken should be recorded.) When was solid food started? Was the baby given any vitamin drops? If yes, in what dosage, how frequently and for how long?
Details of food intake in an older child	What were the amount and frequency of food intake in the last 24 hours? (The details of the quantity and quality of the food taken should be recorded.) Was it cooked properly? Was the child given any vitamin supplements? If yes, in what dosage, how frequently and for how long?

Table 2.11 outlines the routine immunisation schedule for children at different ages according to UIP. Additional vaccinations include MMR (measles, mumps and rubella) and booster dose of TT (tetanus toxoid). MMR vaccine can be given by the age of 15–18 months, in the dosage of 0.5 mL subcutaneously. Booster dose of TT should be given at the ages of 10 and 15 years (0.5 mL intramuscularly). Varicella and hepatitis A vaccines are also available but are not recommended for routine use.

Ask whether any optional vaccines were given to the child. If so, details of each immunisation should be noted. If the age of the child is less than 5 years, details of pulse polio immunisations should be enquired.

PERSONAL HISTORY

Personal history is relevant if the child is above 7 years of age. It includes various aspects of the child's personal habits, attitude and interaction with others. It can be relevant, for instance, in anticipating vitamin B_{12} deficiency in a child with strict vegetarian diet. Information about the attitude and interaction with others may be derived from the child's school performance or ability to make friends.

Sample leading questions to elicit the personal history

- What are the eating, sleeping, bowel and bladder habits like?
- Is he/she a difficult child?
- Is he/she negativistic?
- Is he/she outgoing? Can he/she make friends easily?
- Is there a history of breath-holding spells, tics or temper tantrums?
- Does he/she have any food fads (strong like or dislike for particular food items)?

HISTORY OF ALLERGY

The examiner should enquire about the history of allergy in the child. This could include skin, nasal, respiratory or gastrointestinal allergy. Any allergy to particular food items or medication should also be documented. Few children may develop rashes after eating particular foods such as fish. Allergy can manifest in the form of skin rashes, vomiting, diarrhoea, wheezing, breathlessness, anaphylaxis, shock, etc. It may also result in sudden death.

TABLE 2.11 Immunisation Schedule with Timing, Dosage and Route of Administration

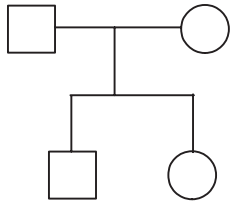
Age	Vaccine	Route	Dose	Site
At birth	Polio	Oral	2 drops	Oral
At birth (before 1 year)	BCG	Intradermal	0.1 mL	Left deltoid
45 days (6 weeks)	DPT	Deep intramuscular	0.5 mL	Anterolateral aspect of thigh
	Polio	Oral	2 drops	Oral
75 days (10 weeks)	DPT	Deep intramuscular	0.5 mL	Anterolateral aspect of thigh
	Polio	Oral	2 drops	Oral
105 days (14 weeks)	DPT	Deep intramuscular	0.5 mL	Anterolateral aspect of thigh
	Polio	Oral	2 drops	Oral
9 months (270 days)	Measles	Subcutaneous	0.5 mL	Right upper arm (deltoid)
18 months	DPT (I booster)	Deep intramuscular	0.5 mL	Anterolateral aspect of thigh
	Polio	Oral	2 drops	Oral
4–5 years	DT (II booster)	Deep intramuscular	0.5 mL	Anterolateral aspect of thigh
	Polio	Oral	2 drops	Oral

FAMILY HISTORY

The family history has a strong bearing on the disease propensity of the individual. Many diseases result from genetic causes inherited from the parents. Certain beliefs, customs and habits are also acquired from the family. Communicable diseases tend to spread faster in families. Important aspects of family history include the following:

1. *Age of the parents*: The incidence of certain diseases increases with advancing age of the parents at the time of birth of the child (Table 2.12).
2. *Consanguinity*: Diseases with autosomal-recessive pattern of inheritance are common in the children born to the parents with consanguineous marriage. The degree of consanguinity and its effect on expression of autosomal-recessive conditions are detailed in Table 2.13.
3. *Family tree (pedigree chart)*: This is a pictorial depiction of the members of the family using standard symbols. It includes the number of children, their age and gender, marriages, deaths, divorces, abortions, twin-births, etc. A pedigree chart puts all the family members and their lineage relationship in one sheet. It can help identify the inheritable pattern of any condition with greater ease. The standard symbols used to draw the pedigree chart are shown in Fig. 2.1.

   A pedigree chart for a family with two children (one male and one female) born out of non-consanguineous marriage is shown below.



4. *Significant illness in the family members*: The examiner should enquire in a systematic manner about any similar illness in the family (Table 2.14). The family includes grandparents, parents, brothers, sisters, cousins, uncles and aunts, both on the maternal and on the paternal sides. This is relevant because of the following

TABLE 2.12 Diseases Due to Advancing Age of Parents

Advanced Age	Disorders
Mother	CNS anomalies Down's syndrome Mental subnormality Premature labour Dizygotic twins
Father	Marfan's syndrome Apert's syndrome (craniostenosis with syndactyly) Achondroplasia Osteogenesis imperfecta Congenital deafness Congenital heart diseases Down's syndrome associated with fusion of chromosomes 21 and 22

TABLE 2.13 Degrees of Consanguinity

Degree of Consanguinity	Definition	Common Genetic Makeup Between Parents
I degree	Marriage between brother and sister. This never occurs in India. The sexual relationship between the brother and the sister is known as incest	50% genetic material in common. Probability of expression of autosomal-recessive conditions is maximal
II degree	Marriage with the father's own sister or mother's own brother	25% genetic material in common
III degree	Marriage with father's sister's son or daughter or mother's brother's son or daughter. This type of marriage is more common in India	12.5% genetic material in common
IV degree	This type of marriage is between distant relatives	Minimal risk of autosomal-recessive diseases amongst consanguineous couples

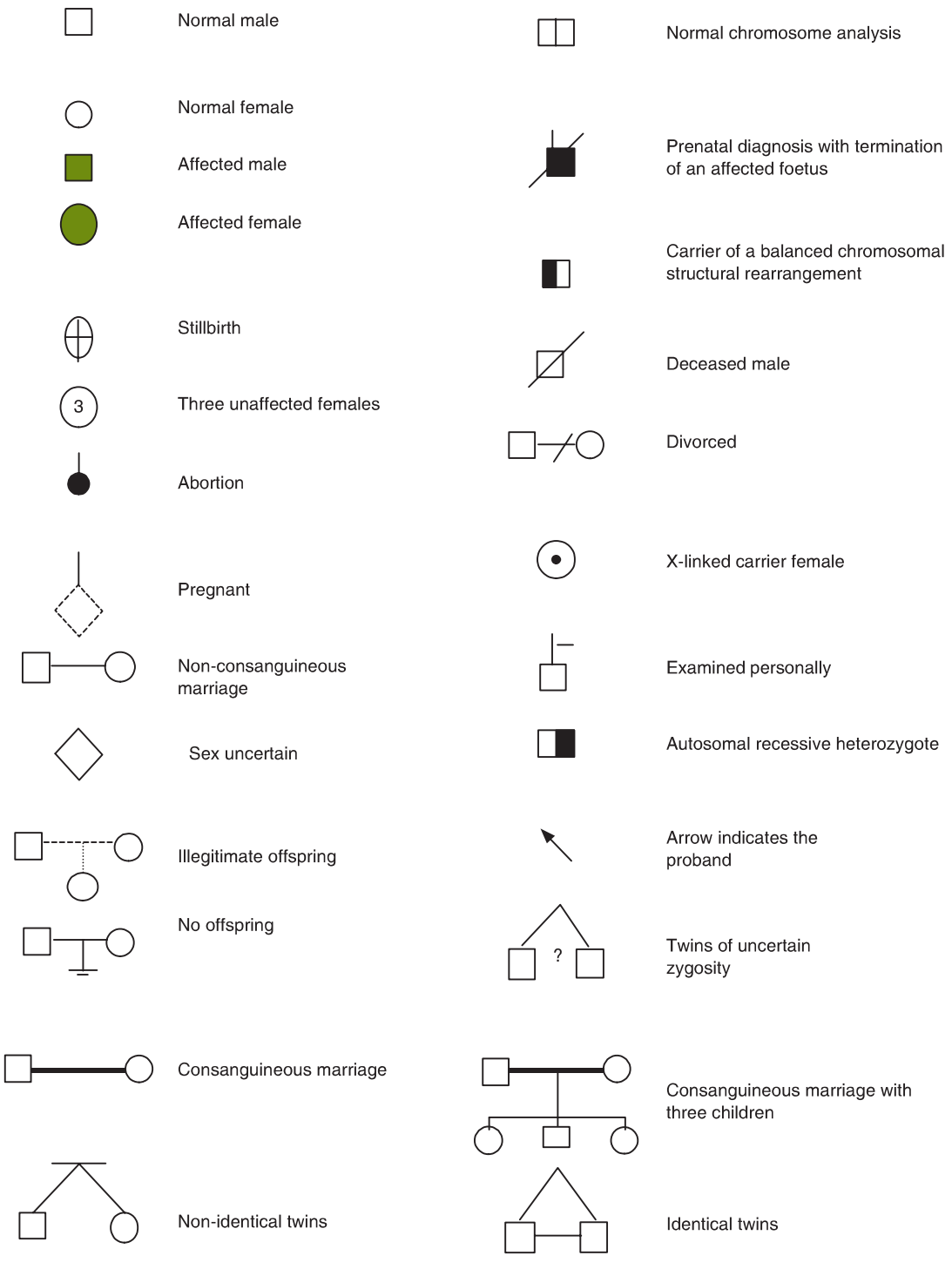


FIGURE 2.1 Symbols commonly used in drawing a pedigree chart.

reasons:

- Certain inheritable conditions such as congenital cardiac defects or seizure disorders tend to run in families. For a suspected inheritable condition, the examiner should draw a detailed pedigree chart to note its pattern of occurrence.
- Any contagious condition is more likely to spread among those members of the family who are in close contact with each other. This is especially applicable to diseases with high secondary attack rate.
- Certain customs, habits, social taboos and food fads are also learnt or acquired from family members. The examiner should especially enquire about bad child-rearing practices that may have led to the present illness (Table 2.15).

5. *Family history relevant to nutrition*:
   - Occupation of the parents—whether mother is working
   - Whether broken family or single parent
   - Literacy of the parents
   - Was the child separated from the mother or parents?
   - Whether the mother is pregnant or not

TABLE 2.14 Relevant Family History According to Body Systems

Body System	Relevant Family History
Cardiovascular system	Incidence of congenital heart defect is more when other family members (especially siblings) are suffering from congenital heart defects Incidence of rheumatic fever is more common in the close contacts within the family A baby born to a diabetic mother is more prone to develop congenital heart defects (commonly asymmetrical hypertrophy of the interventricular septum) Sudden unexpected death of infants in the family may be associated with cardiac disorders
Central nervous system	Seizures and degenerative disorders are more common in the families with a positive history of similar illness[a]
Gastrointestinal system	Jaundice, metabolic disorders, Wilson's disease
Genitourinary system	Polycystic kidney, renal stones, hereditary nephritis, nephrogenic diabetes insipidus and congenital nephritic syndrome

[a]One should be careful in interpreting the history of convulsions. Even in functional (hysterical) convulsions, there may be a positive family history. A child who has observed any family member with convulsions may exhibit the same type of abnormal movements without any CNS involvement.

TABLE 2.15 Bad Child-Rearing Practices and Their Effects

Bad Child-Rearing Practices	Effects
In certain families, female children are not allowed to go out of the house	These children are prone to develop rickets due to lack of exposure to sunlight
Prelacteal feeds and bottle feeding	The child is deprived of the beneficial effects of breastfeeding and is more prone to gastrointestinal infections
Application of cow dung on the cut surface of umbilical cord	Increases the risk of tetanus
Instillation of oil in the nose	Increases the risk of aspiration and pneumonia
Ingestion of neem oil with the belief that it will clean the gut	Neem oil poisoning
Burning of incense	Chemical pneumonitis
Branding for jaundice	Infection
Starvation during diarrhoea	Malnutrition
Overfeeding/junk feeds	Predisposes to obesity and hypertension
Dresses covering whole of the body	Rickets

SOCIAL AND ENVIRONMENTAL HISTORY

The social and environmental milieu also dictate the susceptibility of the child to any disease or condition. The examiner should consider the following aspects while assessing the social and environmental history:

1. *Socioeconomic status*: The socioeconomic status can be classified, according to the occupation, into the following five classes:
   - Class I—executives, judges and collectors
   - Class II—professionals such as doctors
   - Class III—trained workers
   - Class IV—untrained workers
   - Class V—street dwellers
2. *Per capita income:* Per capita income of the family is calculated by adding the total income of all the earning members and dividing it by the number of family members. The examiner should also enquire about the portion of this income spent on food.

$$\text{Per capita income} = \frac{\text{total income of the family}}{\text{number of family members}}$$

3. *Housing conditions*:
   - Housing type—thatched/pukka
   - Living area per person—number of rooms, any overcrowding
   - Ventilation facilities—adequate/not adequate
4. *Water source*:
   - Water supply to the house—well/tap water/bore well
   - Water-cleaning facilities—boiled/filtered/any other/none
5. *Sewage disposal*:
   - Sanitation facilities—toilet facilities/open air defaecation
   - Hygiene status—distance from water source, hand washing followed/not followed
6. *Environment*:
   - Pollution due to vehicle smoke predisposes to lead poisoning
   - Factories letting out harmful substances such as lead may predispose to lead poisoning
   - Contamination of water predisposes to infections and poisoning

Kuppuswamy's Socioeconomic Status Scale

Another method of assessing the socioeconomic status is Kuppuswamy's socioeconomic status scale, which takes into consideration the education status, occupation and family income. This scale was put forth in 1976 and was modified in 1998 and 2007.

Scorecard

(A) Education

Education	Score
Professionals or honours	7
Graduate or postgraduate	6
Intermediate or post high school diploma	5
High school certificate	4
Middle school certificate	3
Primary school or literate	2
Illiterate	1

(B) Occupation

Occupation	Score
Profession	10
Semiprofession	6
Clerical, shop owner, farmer	5
Skilled worker	4
Semiskilled worker	3
Unskilled worker	2
Unemployed	1

(C) Family Income Per Month (Rs)

Family income per month (Rs)—original	Score	Family income per month (Rs)—modified for 2007
≥2000	12	≥19575
1000–1999	10	9788–19574
750–999	6	7323–9787
500–749	4	4894–7322
300–499	3	2936–4893
101–299	2	980–2935
≤100	1	≤979

Socioeconomic class			Total score (A+B+C)
Upper		I	26–29
Middle	Upper middle	II	16–25
	Lower middle	III	11–15
Lower	Upper lower	IV	5–10
	Lower	V	<5

CHAPTER 3

Physical Examination in Children

Physical examination of a child involves a complete head-to-foot examination, including all the systems with special emphasis on the area most probably affected, as per the history taken. It usually begins with an inspection of the general appearance of the child.

GENERAL APPEARANCE

The general appearance gives valuable information regarding the condition of the child. The examiner should note if the child looks healthy, unwell or ill. It is also important to observe if the child appears comfortable or not.

NUTRITIONAL STATUS

The nutritional status of the child corroborates with the nutritional history of the child. It may also indicate some chronic diseases or conditions that affect the basal metabolism.

Body mass index (BMI) is a statistical measurement that is calculated as follows:

$$\text{BMI} = \frac{\text{Weight (kg)}}{[\text{Height/length (metre)}]^2}$$

Although BMI does not directly measure the body fat, it is primarily used to assess obesity. It is used to estimate the ideal weight for a particular height.

BMI is widely used to identify whether the patient is underweight, overweight or obese (Table 3.1).

In children and adolescents, BMI more than 25 kg/m^2 is considered as obesity (Table 3.2).

In children and adolescents, age-related standard percentile charts for BMI are used to classify overweight and obesity as given in Table 3.3.

TABLE 3.1 Classification of Nutritional Status According to BMI in Adults

Classification	BMI (kg/m^2)
Underweight	<18.5
Normal	18.5–25
Overweight	25–30
Obesity	30–40
Morbid obesity	>40

TABLE 3.2 Classification of Nutritional Status According to BMI in Children and Adolescents

Classification	BMI (kg/m^2) in Children and Adolescents
Severe undernutrition	<13
Moderate undernutrition	<15
Normal	15–22
Overweight	22–25
Obesity	>25

TABLE 3.3 Classification of Nutritional Status According to Age-Related Percentile Charts for BMI

Nutritional Status	BMI (kg/m^2) for Age
Underweight	<5th percentile
Normal	5th–84th percentile
Overweight	85th–94th percentile
Obese	≥95th percentile

TABLE 3.4 Nutritional Status and Its Implications

Nutritional Status	Definition	Implications
Well nourished	The child weighs appropriate for age, with no signs of nutritional deficiency	Symptoms of nutritional and vitamin deficiencies are not seen
Protein energy malnutrition (PEM)	Range of pathological conditions arising from coincidental lack of varying proportions of proteins and calories	Helps in deciding the management protocol. Grade I PEM can be managed with proper diet while grade III and grade IV PEM require hospitalisation
Overweight	BMI is more than 85th percentile for age	The child should be managed at this stage itself. With proper diet and health education, the child becomes normal
Obesity	BMI ≥95th percentile for age	Associated with complications such as hypertension, respiratory disorders, diabetes, etc.

Table 3.4 depicts a few nutritional conditions and their implications.

CONSCIOUSNESS

Consciousness is a person's awareness of self and surroundings. The examiner should note the level of the child's consciousness and grade it accordingly. Table 3.5 outlines various altered levels of consciousness.

Glasgow Coma Scale

This neurological tool is used to record the conscious state of a person for initial as well as subsequent assessments. Its advantage is that it is a reliable and objective tool that can be used even by less trained personnel.

TABLE 3.5 Altered Levels of Consciousness

Level	Features	Identifying Features
Delirium	Clouding of consciousness with attention deficit	Confusion, disorientation, irrationality and excitability
Lethargy	Drowsiness and disinterest in the environment	Responds to verbal calls but has difficulty in maintaining an aroused state
Obtundation	Increase in lethargy	Mentally dulled or blunted, responds only to repeated verbal and painful stimuli
Stupor	State of unconsciousness from which the child can be momentarily aroused	Responds only to deep painful stimuli (such as pressure over the sternum)
Coma	Prolonged and profound unconsciousness	Not responding even to deep painful stimuli

Score	Response
Eye opening	
4	Spontaneously opens the eyes
3	Responds to verbal command
2	Responds to pain
1	No response
Best verbal response	
5	Oriented
4	Confused conversation
3	Inappropriate words
2	Incomprehensible sounds
1	No response
Best motor response	
6	Obeys movement commands promptly
5	Purposeful reaction to painful stimulus (localises painful site)
4	Non-purposeful reaction to painful stimulus (flexion withdrawal)
3	Non-purposeful flexion movements to painful stimulus Abnormal flexion response Decorticate rigidity
2	Extension response to painful stimulus Decerebrate posture
1	No movements after painful stimulus

Values of the eye, motor and verbal responses are added to get a final score. These values are also considered separately. The lowest possible Glasgow Coma Scale score is 3 (deep coma or death), while the highest is 15.

Modified Glasgow Coma Scale

Rapid neurological assessment in children is done by using the Modified Glasgow Coma Scale. The Glasgow Coma Scale was modified in relation to age, as adults and children respond differently to various stimuli.

Score	Infants	Children
Eye opening		
4	Spontaneously	Spontaneously
3	To verbal command	To speech/verbal stimuli
2	To pain only	To pain only
1	No response	No response
Motor response		
6	Spontaneous and purposeful movements	Obeys commands
5	Withdraws to touch	Localises painful stimulus
4	Withdraws in response to painful stimulus	Withdraws in response to painful stimulus
3	Abnormal flexion response to pain (decorticate posturing)	Abnormal flexion response to pain (decorticate posturing)
2	Abnormal extension response to pain (decerebrate position)	Abnormal extension response to pain (decerebrate position)
1	No movements after painful stimulus	No movements after painful stimulus
Verbal response		
5	Coos and babbles, smiles, and recognises familiar objects and persons	Oriented and converses appropriately
4	Uncertain recognition of objects or persons and irritable cries	Disoriented and confused
3	Cries in response to pain	Replies inadequately and speaks incoherently using inappropriate words
2	Moans in response to pain	Makes only incomprehensible sounds
1	No response	No response

MENTAL AND EMOTIONAL STATE

The mental and emotional state of the child depends on various factors, including the health status. For instance, a sick child will not be interested in the surroundings. By observing the child, the health status may be assessed to some extent. Types of mental and emotional states are as given below:

- Happy, playful, alert and interested in the surroundings (normal healthy child)
- Anxious (anxiety neurosis)
- Elation—a feeling of well-being or excitement (in bipolar mania)
- Euphoria—an exaggerated feeling of well-being often not justified by circumstances
- Depression (depressive psychiatric disorders)
- Restless (hyperactive child and child with pain)
- Dull, not interested in surroundings, apathetic or irritable (in kwashiorkor)
- Shy and timid or obstinate (seen in overprotected child)

INTELLIGENCE

Intelligence is measured in terms of motor, adoptive, language and social behaviour. It reflects the maturity and integrity of the central nervous system (CNS).

The tests for intelligence vary with age and educational status of the child. The intelligence quotient is measured as follows:

$$\text{Intelligence quotient} = \frac{\text{Mental age}}{\text{Chronological age}} \times 100$$

Mental age can be assessed based on the child's performance in the tests. The intelligence quotient

is low in children with cerebral cortical damage. It helps to assess the cortical functions.

STATURE

Normal Stature

The height or length is between 3rd and 97th percentile for age, sex, region and race.

Short Stature

The height or length is below third percentile or less than two standard deviations below the mean for the age, sex, region and race. Causes of short stature are as follows:

- Familial
- Constitutional
- Chromosomal disorders such as Down's syndrome and Turner's syndrome
- Endocrine disorders such as hypopituitarism and hypothyroidism
- Undernutrition
- Chronic systemic disorders
- Psychosocial conditions
- Skeletal dysplasias such as achondroplasia
- Children born small for gestational age

Tall Stature

The length or height is above 97th percentile or two standard deviations above the mean for normal population of same age, sex, region and race. Causes for tall stature are as follows:

- Constitutional
- Cerebral gigantism
- Marfan's syndrome
- Sexual precocity
- Beckwith–Wiedemann syndrome

DECUBITUS (POSTURE)

Decubitus is the position in which the patient is lying down or sitting. The posture of the patient can provide the examiner with valuable clues to diagnose the underlying disease or condition. Some conditions with their typical postures are given in Table 3.6.

TABLE 3.6 Typical Postures Associated with Diseases or Conditions

Disease/Condition	Associated Posture
Malnutrition	Generalised kyphosis of the dorsal and cervical spine and lordosis of the lumber spine. The child stands on a wide base with mild hyperextension of the knee (asthenic posture)
Acute severe asthma	Stooping forward position
Epiglottitis	Sits upright and leans forward
Pleural effusion	Left lateral decubitus in left-sided pleural effusion and vice versa (child lies on the same side of effusion, so that the fluid does not compress the lungs on the opposite side)
Pleurisy	Lies on the same side of the pleurisy to decrease the movement of the chest
Cyanotic spell	Child assumes a squatting position
Dyspnoea due to cardiac failure	Propped up position with back rest
Peritonitis	Lies quietly with minimal movement
Liver abscess	Lies on the right side to decrease the movements of the liver
Spastic cerebral palsy	Crossing of legs (due to adductor spasm)
Athetoid cerebral palsy	On and off athetoid movements (loosening and stiffening of the body)
Hypotonic cerebral palsy	Pithed frog posture (floppy position, lies still)
Lesion of CNS at the intercollicular level	Upper limbs extended and internally rotated and lower limbs extended (decerebrate rigidity)
Diffuse cortical damage	Arms flexed and legs extended (decorticate rigidity)
Hemiplegia	Poor movements on one side of the body with external rotation of lower limbs
Meningitis	Lies on one side with the spine flexed, neck extended, thighs flexed on the abdomen and legs flexed at knee
Lesion at the brainstem level (elimination of cerebral functions)	Decerebrate posture—stiff, extended extremities, trunk and head; elbow extended; wrist extended; and arms hyperpronated. It indicates that the pontine and vestibular nuclei are maintaining the posture

(Table continued)

TABLE 3.6 *(Continued)*

Disease/Condition	Associated Posture
Lesion above the midbrain	Decorticate posture—elbow flexed, wrist flexed, arms supinated and flexed, clenched fists, and lower limbs rigid and extended. The body position is maintained by the midbrain and red nucleus without inhibition by diencephalon, basal ganglia and cerebral cortex
Tetanus or strychnine poisoning	Bending of the body like an arc (opisthotonos) Pleurothotonos—lateral bending of the body Emprosthotonos—bending in a backward direction

BODY ODOUR

Body odour depends upon the substances secreted in the sweat. In a number of metabolic diseases, these substances give characteristic odour to the body. This often gives a clue to the clinical condition the child is suffering from (Table 3.7).

TABLE 3.7 Typical Breath and Body Odours Associated with Clinical Conditions

Odour	Clinical Condition
Acetone breath	Ketosis
Ammoniacal odour	Uraemia
Boiled cabbage odour	Tyrosinaemia
Cat's urine odour	Multiple carboxylase deficiency
Cheesy or sweaty odour	Isovaleric acidaemia
Fishy odour	Trimethylaminuria
Fetor hepaticus	Liver cell failure
Fruity odour	Alcohol consumption
Garlic-like odour	Phosphorus, arsenic, parathion or malathion poisoning
Halitosis	Bronchiectasis and lung abscess
Maple syrup or burnt sugar odour	Maple syrup urine disease
Mousy odour	Phenylketonuria and hepatic failure
Musty odour	Phenylketonuria
Putrid odour	Suppurative lung disease and bronchiectasis
Sweety odour	Diabetic ketoacidosis
Rancid butter/rotten cabbage odour	Hypermethioninemia

CRY OR VOICE

Normal cry is usually lusty and strong. The way an infant cries or the voice of a child can help the physician diagnose various conditions. For instance, grunting cry is seen in children with alveolar disorders with decreased surfactant. The child cries against partially closed glottis. In any condition with decreased surfactant, the alveoli tend to collapse during expiration. Grunting maintains a positive end expiratory pressure so that alveoli do not collapse during expiration. Table 3.8 lists some normal and abnormal cries and their associated clinical conditions.

TABLE 3.8 Typical Cries Associated with Clinical Conditions

Cry/Voice	Clinical Condition/Possible Cause
Lusty, strong cry (seen in newborn, full-term infants and healthy children)	Hunger Discomfort (e.g., wet diaper or bed)
High-pitched cry	Intracranial pathology such as meningitis, encephalitis and kernicterus
Inconsolable/incessant cry	Infections (e.g., meningitis and bronchopneumonia) Discomfort (e.g., infantile colic and diaper wetting) Ant bite
Grunting cry (expiratory grunt)	Lobar pneumonia, acute bronchiolitis, respiratory distress syndrome in newborn and empyema in children
Whispering, whining or tremulous cry	Kwashiorkor
Stridor (noisy respiration due to obstruction of passage of air in the lower respiratory tract) with a hoarse cry	Congenital laryngeal stridor, vocal cord paralysis, laryngeal web and laryngeal papilloma
Cat-like cry	Cri-du-chat syndrome (deletion of 'p' arm of fifth chromosome)
Intermittent cry	Infantile colic and intussusception (colic with pallor)
Continuous crying	Mental retardation
Hoarse cry (voice)	Cretinism, laryngitis and diphtheria
Loud cry	Anger or temper tantrum
Cry like bleat of a goat	De Lange syndrome
Feeble cry	Acute illness, amyotonia congenita, Down's syndrome and beriberi
Seagull-like cry	Edward's syndrome (trisomy 18)
Masculine voice/cry	Precocious puberty

FACIES

The term *facies* refers to the typical facial expressions associated with certain conditions. The examiner can diagnose a number of conditions by looking at the face of the child. A few important facies and the typical conditions they are associated with are enlisted in Table 3.9 (see also Fig. 3.1).

TABLE 3.9 Typical Facies and Their Associated Conditions

Facies	Condition/Disease
Mongoloid facies—round face and head with flat occiput, mongoloid slant of the eyes, epicanthic folds and thick, large, protruding tongue	Down's syndrome
Cushingoid facies—moon face with fish mouth, prominent flushed cheeks, double chin and buffalo hump	Cushing's syndrome
Apathetic moon face associated with irritability	Kwashiorkor
Expressionless face	Bilateral facial nerve palsy
Elfin facies—broad, high, receding forehead; hypertelorism; strabismus; epicanthic folds; low set ears; upturned nose; long upper lip; wide mouth; and pointed chin with dental abnormalities such as small teeth	William's syndrome
Haemolytic facies—puffy face with frontal and parietal bossing in a child 2–3 years of age	Thalassaemia and other haemolytic anaemias
Lethargic face with sunken, dry eyes associated with a weak cry	Severe dehydration
Pinched facies (loss of subcutaneous fat), old-man appearance, sunken eyes with hollow cheeks and temples in an alert child who is interested in the surroundings	Marasmus
Adenoid facies—open mouth, narrow pinched nose, short upper lip, eversion of the lower lip and dull facial expression associated with mouth breathing	Chronic nasal obstruction commonly due to adenoid enlargement
Blank and unresponsive facies	Mental retardation
Cretinoid facies—thick, heavy face with a dull look; thick eyebrows; and thick protruding tongue	Hypothyroidism
Risus sardonicus—appearance of a sardonic grin due to down and out pull on the corners of the mouth, with the upper lip stretched across. Eyes are slit like and puckered up, with the eyebrows drawn upwards	Tetanus
Gargoylism—coarse facies, thick lips, low set ears, depressed nasal bridge and enlarged tongue with peg-like teeth that are widely separated	Mucopolysaccharidosis
Potter facies—widely spaced eyes, depressed nasal bridge, receded chin, and ears asymmetrical, low set, floppy and posteriorly rotated	Bilateral renal agenesis (resulting in oligohydramnios)
Doll-like facies	Glycogen storage disorders
Hepatic facies	Liver failure
Triangular face	Watson–Alagille syndrome
High forehead and hypertelorism	Zellweger syndrome (hepatocerebrorenal syndrome)

SKULL

Size of the Head

Any deviation in the size and proportion of the head should be noted.

Macrocephaly

Macrocephaly is defined as head circumference more than two standard deviations above the mean or beyond 97th percentile for normal population of same age, sex, race and region.

An increase in the head circumference of more than 2 cm per month in the first 6 months should raise suspicion of macrocephaly. Some important causes of macrocephaly with the structures affected are detailed in Table 3.10.

The head of preterm babies may appear disproportionately large. So by clinical appearance alone one should not diagnose macrocephaly



(a) (b) (c)

FIGURE 3.1 Facial appearance in various conditions. (a) Cretinoid facies. (b) Down's syndrome—mongoloid facies, depressed nasal bridge, protruding tongue, low set ears and short neck. (c) Haemolytic facies.

TABLE 3.10 Structure-Wise Depiction of Causes of Macrocephaly

Structures Affected	Causative Disease/Condition
Skull (macrocrania)	Haemolytic anaemia Osteopetrosis Achondroplasia
Subdural space	Subdural effusion/haematoma
Subarachnoid space	Hydrocephalus
Brain parenchyma	Megalencephaly with increased brain growth, as in Sotos' syndrome (cerebral gigantism)
Vessels	Vein of Galen malformation
Ventricles	Hydrocephalus
Miscellaneous	Intracranial tumours Arachnoid cysts Neurofibromatosis Infiltrations—mucopolysaccharidoses (Hurler's syndrome), Tay–Sachs disease and generalised gangliosidoses Hydranencephaly—cerebral hemispheres are not developed; meninges and skull are normal

unless confirmed by anthropometry. A thorough physical examination is necessary as is evident from the following example. In hydrocephalus that is associated with Dandy–Walker cyst, the occiput will appear prominent. If hydrocephalus is associated with Arnold–Chiari malformation, the occiput will not be prominent. Macrocephaly, if present, should be appropriately investigated.

Megalencephaly or Macrencephaly

Megalencephaly or macrencephaly is a condition where the weight and size of the brain are more than average for the age and sex of the child. This condition may later present as macrocephaly, as the enlarged brain pushes the cranium.

Age group	Normal brain weight (g)
Newborn	350–400
At about 3 years	1000–1080
6–12 years	1300–1350
Adult	1300–1400

The weight of the enlarged brain can even be more than 1800 g in some patients with megalencephaly. Megalencephaly may be seen in the following conditions:

- Normal children with extraordinary intelligence
- Cerebral gigantism (Sotos' syndrome)
- Neurocutaneous syndromes—tuberous sclerosis, neurofibromatosis and Sturge–Weber syndrome
- Metabolic disorders—leukodystrophy, lipidosis, histiocytosis and mucopolysaccharidosis

Megalencephaly may or may not be associated with altered functions of the brain. Common symptoms are delayed development, seizures and corticospinal dysfunction.

Microcephaly

Microcephaly is defined as head circumference less than three standard deviations below the mean for



FIGURE 3.2 Microcephaly.

the age, sex, race and region (Fig. 3.2).

Microcephaly may be primary or secondary. Primary microcephaly is present since birth and the causes are inherited. Secondary microcephaly occurs due to an insult to the growing brain, which results in deceleration or arrest of brain growth. The differentiating features are listed in Table 3.11.

For more information on causes of microcephaly, see Chapter 11.

Shape of the Head

The shape of the head depends on the shape of the skull. Abnormal skull shapes (Fig. 3.3) result from craniosynostosis, a condition in which there is a premature fusion of the cranial sutures. It may also be seen secondary to decreased brain growth.

Cephalic index is the ratio of the maximum width of the head multiplied by 100 divided by its maximum length. This index is helpful in diagnosing various skull shapes related to conditions such as brachycephaly and scaphocephaly.

Length–width index or length–breath index (Table 3.12):

$$\text{Length–width index} = \frac{\text{Maximum cranial width}}{\text{Maximum cranial length}} \times 100$$

This index is useful in determining the type of cranium when there is a doubt regarding its type from the appearance.

Trigonocephaly is triangular in appearance and plagiocephaly is asymmetrical in appearance. Hence,

TABLE 3.11 Differences between Primary and Secondary Microcephaly

Features	Primary/Familial Microcephaly	Secondary Microcephaly
Appearance	Low crown, receding forehead, occipital flattening and wrinkling of skin	Small head
Onset	Present since birth	May be present at birth or evident later (by the first year)
Predisposing cause	No predisposing cause	Malnutrition, systemic illness, TORCH infections, alcohol, drugs (antiepileptic and antimalignancy drugs), drug addiction (marijuana, cocaine and heroin), hyperthermia and hypothyroidism in the mother
Causes	Chromosomal anomalies • Autosomal recessive/dominant disorders • Sex-linked (may be associated with spastic diplegia) Examples are Down's syndrome, craniosynostosis, Pelizaeus–Merzbacher disease, Smith–Lemli–Opitz syndrome, Rubinstein–Taybi syndrome, Batten disease	Cerebral dysgenesis/hypoplasia Infections—TORCH infections (congenital) and meningitis (acquired) Hypoxia/anoxia Hypothyroidism in the newborn Foetal alcohol syndrome Foetal hydantoin syndrome Malnutrition due to decreased food intake by the child Metabolic disorders (phenylketonuria) Trauma—birth injuries

TABLE 3.12 Appearance and Length–Width Index of Various Types of Crania

Type of Skull	Appearance	Length–Width Index
Turricephaly	High peaked	>85
Oxycephaly	High and sloping	>85
Brachycephaly	Short cranium	80–85
Mesocephaly	Normal cranium	60–75
Dolichocephaly	Long cranium	70–75
Scaphocephaly	Canoe-shaped cranium	<70

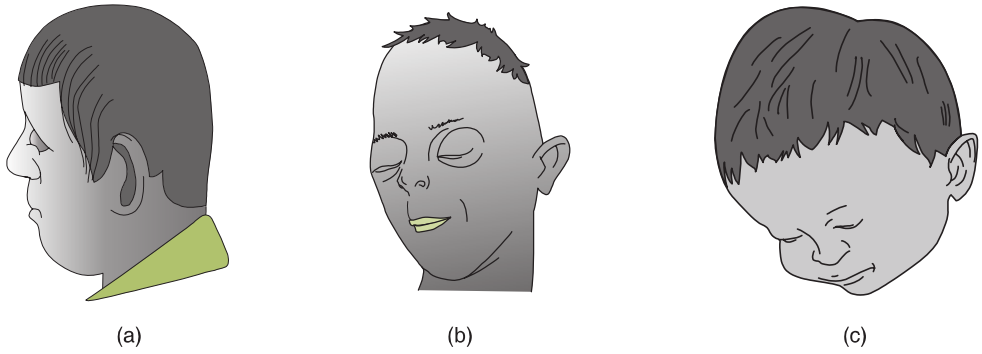


FIGURE 3.3 Abnormal skull shapes. (a) Brachycephaly. (b) Oxycephaly. (c) Plagiocephaly.

the length–width index is not significant in these conditions.

Various abnormal shapes of the head are as follows:

1. *Dolichocephaly or scaphocephaly*: In this condition, the anteroposterior length of the skull is more than its width so that the skull appears boat-shaped (Fig. 3.4). This condition results from the anteroposterior growth of brain due to premature fusion of the sagittal suture while the coronal and lambdoid sutures allow growth. It is associated with a prominent occiput and broad forehead with small or absent anterior fontanel. As the anteroposterior diameter is more, there is a history of cephalopelvic disproportion during labour.
2. *Brachycephaly*: In this condition, the coronal suture fuses prematurely. The brain grows sidewards causing broadening of the skull, flat forehead and decreased anteroposterior diameter. Brachycephaly is seen in certain conditions such as the following:
   - Apert's syndrome
   - Carpenter's syndrome
   - Crouzon's syndrome
   - Down's syndrome
3. *Trigonocephaly*: In this condition, the metopic suture, which is present between the two frontal bones, fuses prematurely. Hence, the skull is narrow anteriorly and wide posteriorly. This results in an abnormal keel-shaped forehead and hypotelorism. These children are at risk of suffering from developmental anomalies of the fore brain.
4. *Oxycephaly/acrocephaly/turricephaly* (hypsicephaly or high skull, steeple head, tower head and turret skull): In this condition, there is premature fusion of coronal and lambdoid sutures. Skull is abnormally high and conical in shape, and appears like a tower. There is a steep ascent of the parietal and frontal bones. It is often associated with syndactyly. Oxycephaly is seen in children with Crouzon's disease and Pfeiffer's syndrome.
5. *Plagiocephaly*: In this condition, the skull is abnormal and asymmetrical in shape. It occurs due to irregular, asymmetric fusion of sutures. Moulding of skull during delivery resembles plagiocephaly, where the skull is asymmetrical due to pressure effects but does not persist into



FIGURE 3.4 Scaphocephaly.

adulthood. It is seen in children with Chotzen's syndrome. Plagiocephaly may be of two types:

- *Frontal plagiocephaly:* This condition is characterised by unilateral flattening of the forehead, elevation of ipsilateral orbit and eyebrow and a prominent ear on the corresponding side. It is usually associated with a bony bulge on contralateral parietal vault. This condition results from premature fusion of unilateral coronal and sphenofrontal sutures.
- *Occipital plagiocephaly:* This condition is characterised by occipital flattening and bulging of the ipsilateral frontal bone. It is usually due to faulty positioning during the infancy, leading to the fusion or sclerosis of unilateral lambdoid sutures.

6. *Kleeblattschadel deformity:* This condition refers to a trilobed skull, which resembles a cloverleaf. Such skull deformity is caused by premature fusion of multiple sutures. The skull has very prominent temporal bones and the remainder of the cranium is constricted. It is seen in association with Carpenter's, Crouzon's, Apert's and Pfeiffer's syndromes.

Fontanels

These are wide areas of fibrous tissue found at the junction of two or more sutures. There are six fontanels at birth (Figs. 3.5 and 3.6):

1. Anterior fontanel

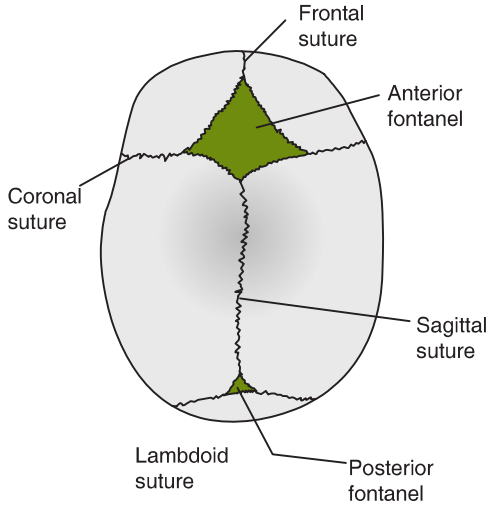


FIGURE 3.5 Normal skull showing fontanels and sutures.

2. Posterior fontanel
3. Two anterolateral—pair of sphenoidal fontanels
4. Two posterolateral—pair of mastoid fontanels

Anterior fontanel is the largest and most important fontanel. Sphenoidal fontanels are found at the junction of temporal and coronal sutures. They are seen anteriorly between sphenoid, parietal, temporal and frontal bones. Mastoid fontanels are present at the junction of temporal and lambdoid sutures. They are seen posteriorly between temporal, occipital and parietal bones. A third fontanel is situated in between the anterior and posterior fontanels in children with hypothyroidism and Down's syndrome.

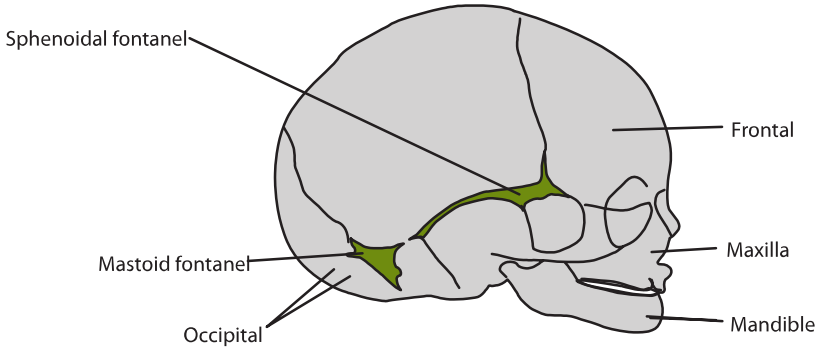


FIGURE 3.6 Sphenoidal and mastoid fontanels.

Anterior Fontanel

Anterior fontanel is a rhomboid-shaped area present at the vertex of the skull where the posteromedial part of both the frontal bones and the anteromedial part of both the parietal bones meet. It is measured by the lines joining the midpoints of the opposite sides, as shown in Fig. 3.7.

The shape, size and time of closure of the anterior fontanel vary widely. The average diameter of the anterior fontanel in an infant is 2.1 x 2.1 cm. The size may vary from 0.6 to 3.6 cm. It may be up to 4 or 5 cm in some normal infants and may even enlarge in the first few months of life. A small fontanel may occur in infants with slow brain growth and craniosynostosis. The usual time of closure of the anterior fontanel is 7–19 months of age. Conditions associated with early closure of anterior fontanel include the following:

- Craniostenosis or craniosynostosis
- Primary microcephaly

Delayed closure of anterior fontanel is seen in the following conditions:

- Achondroplasia
- Apert's syndrome
- Cleidocranial dysostosis (Fig. 3.8)
- Congenital hypothyroidism
- Congenital rubella syndrome
- Congenital syphilis
- Cutis laxa
- Ligamentous laxity
- Delayed development syndrome
- Down's syndrome
- Hallermann–Streiff syndrome (brachycephaly, bird-like facies, bilateral microphthalmos, cataracts, micrognathia with double chin, and hypotrichosis of scalp and eye brows)
- Hydrocephalus
- Hypophosphatasia
- Cretinism or congenital hypothyroidism
- Intrauterine growth retardation
- Malnutrition
- Mucopolysaccharidoses
- Osteogenesis imperfecta
- Preterm infants
- Progeria (premature aging)
- Pyknodysostosis
- Rickets
- Russell–Silver syndrome
- Skeletal dysplasia
- Syphilis
- Thalassaemia major
- Trisomy 13
- Trisomy 18

The configuration of the fontanel (sunken or bulging) can help the examiner in diagnosing many clinical conditions. Although a slight depression of the fontanel is common in normal infants, a *sunken fontanel* is a sign of dehydration in infants. On palpation, a sunken anterior fontanel is slightly depressed relative to the frontal and parietal bones.

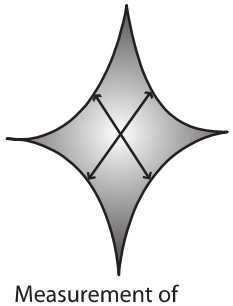


FIGURE 3.7 Method of measuring the anterior fontanel.

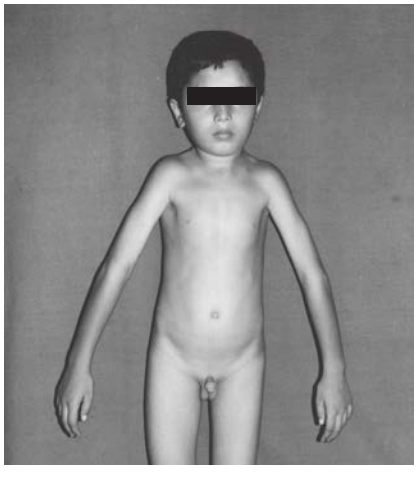


FIGURE 3.8 Cleidocranial dysostosis. Note the absence of clavicle on both sides.

A *bulging fontanel* needs to be differentiated from the normal fullness of the fontanel. A normal fullness may be seen in healthy infants when they cry or are held upright. However, the fontanel in healthy infants is pulsatile. In infants with true bulging of the fontanel (e.g., hydrocephalus), the bulge remains constant in all positions and no pulsations are visible. The most common cause of a bulging fontanel in the neonatal period is intraventricular haemorrhage. Causes of bulging fontanel in an infant include the following:

- Bleeding secondary to whiplash or shaking abuse
- Vitamin D-dependent rickets
- Enzyme defects in urea cycle
- Galactosaemia—a bulging fontanel and jaundice in a young infant suggest the possibility of galactosaemia
- Hyperparathyroidism
- Rubella
- Hydrocephalous
- Hypophosphatasia
- Intracranial tumours
- Increased intracranial tension
- Immunisation—after immunisation with DPT vaccine
- Maple syrup urine disease
- Meningitis—a bulging fontanel may be the only clinical indication in early stages
- Obstruction of a cerebrospinal fluid shunt
- Physiological—transient, unexplained, benign bulging of the fontanel may occur in some normal infants
- Pseudohypophosphatasia
- Pseudotumour cerebri due to vitamin A poisoning, outdated tetracyclines, nalidixic acid, dexamethasone, acetazolamide and oral glycerol
- Subdural haematoma

Posterior Fontanel

Posterior fontanel is present at the point where the lambdoid and sagittal sutures unite. It is triangular in shape and is situated at the junction of the occipital and two parietal bones. At birth, the average size of the posterior fontanel is about 0.5–0.7 cm. It closes completely by 2 months of age. It may be open in Down's syndrome.

Other fontanels are usually not examined as they fuse in utero.

Sutures

Sutures are fibrous septa between the cranial membranous bones. During infancy, cranial bones grow predominantly at their borders. Interference in such growth, as in premature craniosynostosis, seriously hampers normal enlargement of the cranial vault and may lead to cranial distortion. Various sutures present in the skull are as follows (Fig. 3.5):

- Sagittal
- Coronal
- Frontal or metopic
- Lambdoid

Moulding

Overlapping of bones of skull occurs during birth. This is called moulding and is seen immediately after birth in a normal newborn.

Cranial Bossing

Cranial bossing is characterised by rounded prominences at the centre of the parietal and frontal bones. It may occur in infants as an early manifestation of rickets.

Craniotabes

Craniotabes refers to thin, parchment-like soft areas that can be indented like a ping-pong ball. It is more commonly seen along the suture lines and in the parietal bones. It may be physiologically present up to 3 months of age. Other causes of craniotabes are as follows:

- Rickets
- Hydrocephalus
- Hypervitaminosis A
- Osteogenesis imperfecta
- Congenital syphilis

Pachycephaly

Pachycephaly refers to abnormal thickness of skull. It is seen in acromegaly.

Tests for Identifying Abnormal Conditions of the Head

The following tests are helpful in identifying various abnormal conditions of the head.

MacEwen's Sign

It refers to a 'cracked-pot' sound on percussion of the skull. It may be present with hydrocephalus, increased intracranial pressure or suture separation. It is also simulated in many normal infants.

Transillumination Test

A torchlight equipped with a rubber cuff is firmly placed on the skull. This test is done in a dark room. Translucency extending beyond 2–2.5 cm in the frontal area or beyond 2 cm in the occipital area is abnormal.

It is seen in hydrocephalus, subdural effusion and subdural haematoma.

Abnormal Head Movements

The head remains steady in children after the age of 4 months when the head control is attained. After this age, any abnormal movement of the head should be noted. The pattern of movement may indicate various medical conditions. Some abnormal head movements are listed below.

Titubation

Titubation is a feature of cerebellar lesions. The head moves sidewards.

Alfred de Musset's Sign

Alfred de Musset's sign is seen in aortic regurgitation. There is a wide pulse pressure. This results in sudden filling and emptying of the carotids, which causes the up and down movement of the head with each heart beat.

Head Bobbing

In infants, head bobbing synchronous with breathing may be a sign of respiratory distress. Head bobbing in such cases indicates the use of the accessory muscles of inspiration. During examination, it is seen that the infant's head, supported by the parent's forearm, bobs forward with each inspiration.

Spasmus Nutans

If head nodding occurs once or twice a second, either up and down or side to side, along with nystagmus, it is known as spasmus nutans. This includes a triad of pendular nystagmus, torticollis and head nodding.

EYES

Examination of the eyes in infants is difficult. Do not open the eyes forcibly. Hold the infant in hands and move the head up and down. The infant will open the eyes. Do not throw light on the eyes for a long time. Examination of the eyes should be done in a systematic, structure-wise manner as given below.

Spacing

Spacing of the eyes refers to the distance between both the eyes. It is measured by inner canthal distance, outer canthal distance or interpupillary distance.

Canthal index is derived from the ratio of the distances between the inner and the outer canthi of both eyes multiplied by 100. The normal canthal index is 33–38.

Interpupillary distance is the distance between the centres of the pupils of both eyes (Fig. 3.9). It is best measured with the child looking upwards. Mean interpupillary distance in children is about 40 mm and in adults 50–75 mm.

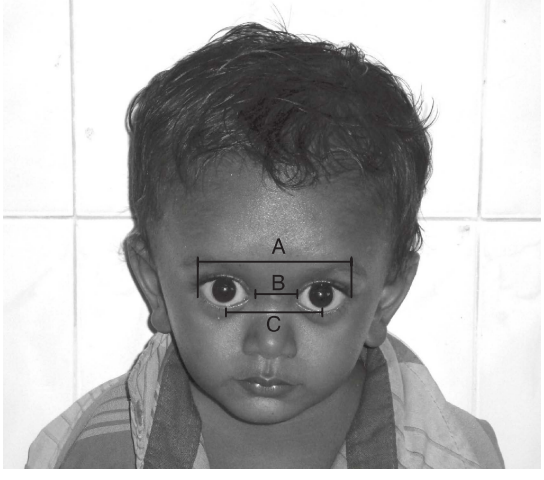


FIGURE 3.9 Spacing of the eyes. A—outer canthal distance. B—inner canthal distance. C—interpupillary distance.

Ocular Hypotelorism

Ocular hypotelorism means that the spacing between the eyes is less than normal. In cases with hypotelorism, the canthal index is less than 33.

Ocular Hypertelorism

Ocular hypertelorism is an abnormally wide spacing of the eyes with a broadened bridge of nose, usually due to maldevelopment of the sphenoid bone (Fig. 3.10). In cases with hypertelorism, the canthal index is more than 38. The causes of ocular hypertelorism include the following:

- Racial variations
- Cretinism
- Cerebral gigantism
- Craniofacial dysostosis
- Orofaciodigital dysostosis
- Thalassaemia major

Several syndromes are commonly associated with ocular hypertelorism. They are as follows:

- Aarskog syndrome
- Apert's syndrome
- Cerebrohepatorenal syndrome
- Chromosome 4p deletion syndrome
- Cri-du-chat syndrome
- Crouzon's syndrome
- Down's syndrome
- Di George syndrome
- Ehlers–Danlos syndrome
- Foetal face syndrome
- Foetal hydantoin syndrome
- Multiple lentigines syndrome
- Noonan's syndrome
- Rubinstein–Taybi syndrome
- Turner's syndrome
- Whistling face syndrome
- William's syndrome

Craniofacial dysostosis is diagnosed by an altered interpupillary distance (the distance between the centres of both the pupils).



FIGURE 3.10 Child with hypertelorism. Also note Harrison's sulcus below right subcostal margin.

Eyebrows and Eyelashes

Examination of eyebrows and eyelashes reveals a lot of information about the conditions the patient may be suffering from. Some of the eyebrow and eyelash changes with the associated conditions are given in Table 3.13.

Eyelids

The examiner should examine the eyelids and their orientation before beginning the examination of the eyes.

Ptosis

Ptosis or blepharoptosis refers to an abnormal drooping of the eyelids. Normally, only about 2 mm of the limbus of cornea is covered by the upper lid when the child looks straight. If more than that is covered by the upper lid, the child is said to have ptosis.

TABLE 3.13 Eyebrow and Eyelash Changes and Associated Conditions

Eyebrow or Eyelash Change	Conditions
Non-pigmented eyebrows and lashes	Albinism
Bushy eyebrows	Hurler's syndrome
Eyebrows meet in the midline—synophrys	Cornelia de Lange syndrome Waardenburg syndrome

It can be unilateral or bilateral. Unilateral ptosis is seen in children with paralysis of oculomotor nerve and Horner's syndrome. Bilateral ptosis occurs in children with defective development of levator palpebrae superioris, myasthenia gravis and myotonic myopathy.

Ptosis can be congenital or acquired. Causes of ptosis are as follows:

1. Congenital
   - Noonan's syndrome
   - Sturge–Weber syndrome
2. Acquired
   - Horner's syndrome
   - Myotonic dystrophy
   - Myasthenia gravis
   - Ocular myopathy
   - Oculomotor nerve palsy
   - Plexiform neurofibromatosis
   - Snake bite (neurotoxic)
   - Tumours of the eyelid
   - Oedema of eyelids

Other Eyelid Disorders

1. *Coloboma* of the eyelid is a notch in the edge of the eyelid. The common site is medial to the midline in the upper eyelids. This is a congenital defect and may be associated with coloboma of iris.
2. *Blepharitis* refers to inflammation of the margins of the eyelids. The lids are erythematous and scaly. It is seen in children with seborrhoea or infections.
3. *Blepharospasm* is an involuntary, sustained and forcible closure of eyelids that can occur spontaneously or in response to a stimulus such as light. It usually presents with excessive blinking and uncontrollable tics or twitches of the eyes.
4. *Lid retraction* is a condition in which the upper eyelid does not cover the upper part of limbus in straight gaze. This condition gives the appearance of a wide-eyed staring look. It is seen in children with hyperthyroidism. It is known as Dalrymple's sign.
5. *Lid lag* is a condition in which the upper eyelid lags behind as the patient looks downwards. It is known as Von Graefe's sign. It usually occurs in thyrotoxicosis.
6. *Lagophthalmos* is present when the patient is unable to close his or her eyes completely. It is seen in patients with hyperthyroidism, ectropion, paralysis of orbicularis muscle, etc.
7. *Infrequent blinking* occurs in thyrotoxicosis. It is known as Stellwag's sign.
8. *Ectropion* is an eversion of the eyelid. The eyelids are rolled outwards. This condition occurs in patients with ulcerative blepharitis due to infection.
9. *Entropion* is an inversion of the eyelid. The eyelids are rolled inwards. This condition occurs due to the following reasons:
   - Spasm of orbicularis muscle in cases with degeneration of the palpebral conjunctiva or
   - Cicatrical contraction of the palpebral conjunctiva.
10. *Xanthelasma palpebrarum* arises due to the deposition of cholesterol underneath the skin around the eyelids.

Horizontal Palpebral Fissure Length

Horizontal palpebral fissure length is the horizontal width of the eye. To measure this length, the examiner should hold a transparent plastic scale in front of the patient's eye across its greatest horizontal axis. Then without touching the eye, with the scale, the examiner should make a note of the measurements (points) corresponding to the medial and lateral canthi. The distance between these points measures the length of horizontal palpebral fissure.

Short palpebral fissures are seen in the following cases:

- Foetal alcohol syndrome
- William's syndrome
- Whistling face syndrome
- Chromosome 10p deletion syndrome
- Microphthalmia

Slanting

Slanting of the eyes refers to the difference in levels between the inner and outer canthi of the eyes. The eyelids may be slanted upwards or downwards.

Mongoloid Slant

Slanting downwards from lateral to medial canthus is known as mongoloid slant. This refers to an upward slanting of the eyes (the outer canthi lie above the line joining the inner canthi). Mongoloid slant is commonly seen in the following cases:

- Down's syndrome
- Prader–Willi syndrome (mongoloid slant with almond-shaped eyes)
- Aarskog syndrome
- Ectodermal dysplasia
- Mongolian race

Antimongoloid Slant

Antimongoloid slant refers to a downward slanting of the eyes. The outer canthi lie below the line joining the inner canthi. Antimongoloid slant is commonly associated with the following disorders:

- Alport's syndrome
- Apert's syndrome
- Alagille syndrome
- Cri-du-chat syndrome
- Crouzon's syndrome
- Noonan's syndrome
- Pfeiffer's syndrome
- Chromosome 10p deletion syndrome
- Smith–Lemli–Opitz syndrome
- Treacher–Collins syndrome
- Trisomy 18
- Turner's syndrome
- Whistling face syndrome

Epicanthus

Epicanthus is a fold of skin extending downwards from the upper lid to cover the inner canthus of the eye. It is normally present in newborn babies but disappears by 1–3 months of age. It is also seen in Mongolian race. Epicanthic fold gives a false appearance of increased distance between the two eyes. These folds are usually seen in the following conditions:

- Cerebrohepatorenal syndrome
- Cri-du-chat syndrome
- Cornelia de Lange syndrome
- Down's syndrome
- Ehlers–Danlos syndrome
- Foetal alcohol syndrome
- Fragile X syndrome
- Hydantoin syndrome
- Leopard syndrome
- Moebius syndrome
- Noonan's syndrome
- Pompe disease (glycogen storage disorder type II)
- Smith–Lemli–Opitz syndrome
- Trisomy 13
- Turner's syndrome
- Unilateral epicanthic fold may be seen in children with torticollis
- William's syndrome

Position and Size of the Eyeballs

The position and size of an eyeball with respect to the orbit and in relation to the other eyeball give information about many ocular as well as systemic conditions.

Proptosis

Proptosis is a forward protrusion of the eyeballs. This condition generally occurs when the size of the orbit is decreased or the size of the eyeball is increased. The following conditions may lead to proptosis due to diminished orbital volume:

- Apert's syndrome
- Arteriovenous (AV) aneurysm
- Cavernous sinus thrombosis
- Craniosynostosis
- Crouzon's syndrome
- Neurofibromatosis—the proptosis in this condition occurs due to an overgrowth of the greater wing of sphenoid. It is pulsatile and becomes more prominent on standing
- Orbital cellulitis/abscess/haemorrhage
- Optic nerve tumours (e.g., optic glioma)
- Retro-orbital tumour or abscess
- Space-occupying lesions of the orbit—secondary deposits in the orbit (e.g., neuroblastoma)
- Thyrotoxicosis (Grave's disease)

Proptosis due to an increased eyeball size is seen in the following conditions:

- Buphthalmos (infantile glaucoma)
- Tumours of the eye (e.g., retinoblastoma)
- Apparent proptosis in cases with high myopia

Enophthalmos

Enophthalmos is a condition where there is a recession of the eyeball back into the orbit. This occurs in the following conditions:

- Horner's syndrome
- Fracture of the bone in the floor of the orbit
- Mechanical retraction by fibrous tissue following orbital cellulitis

Microphthalmos

Microphthalmos is a condition in which the eyeballs are abnormally small in size. It is seen in the following conditions:

- Hallermann–Streiff syndrome
- Patau's syndrome (trisomy 13)
- Edward's syndrome (trisomy 18)
- Diamond–Blackfan syndrome

It is distinct from anophthalmos, which is a congenital absence of one or both eyes (Fig. 3.11).

Strabismus

Strabismus (squint) is non-parallelism of the visual axis in various fields of gaze so that both the eyeballs are not aligned in the same direction. It may be present in most of the waking hours (frank strabismus or tropia) or may be intermittent (phoria—tendency to strabismus).



FIGURE 3.11 Anophthalmos.

TABLE 3.14 Types of Strabismus

Condition	Presentation
Esotropia	Convergent strabismus (eye turns medially)
Exotropia	Divergent strabismus (eye turns laterally)
Hypertropia	Upward deviation of the eye
Hypotropia	Downward deviation of the eye
Esophoria	Tendency to converge
Exophoria	Tendency to diverge

Table 3.14 lists the various types of strabismus and their presentations.

Predisposing Conditions

1. Hereditary factors
2. CNS
   - Cerebral injury (encephalitis, tuberculous meningitis and intracranial haemorrhage)
   - Tumours (intracranial and intraorbital) lead to increased intracranial pressure. This leads to pressure effect on the abducent nerve
   - Guillain–Barre syndrome
3. Ocular
   - Different refractory power in both eyes
   - Impairment of fusion ability due to muscular defects or nerve palsies
4. Miscellaneous
   - Lead poisoning

Transient strabismus may be seen in children with hypoglycaemia.

Nystagmus

Nystagmus is a rhythmic, usually rapid movement of the eyes that may be horizontal, vertical, rotary or mixed. It occurs due to a disturbance in ocular fixation.

To elicit nystagmus, observe the eye with the eyeballs kept straight for about 5 seconds. Again observe with a lateral gaze position. Extreme lateral gaze should be avoided as it will cause nystagmus even in normal children.

Types

1. Types of nystagmus based on the types of movement are as follows:

(a) *Pendular nystagmus*: It refers to the horizontal oscillation of equal amplitude on both sides. Pendular nystagmus occurs when the child looks straight.
(b) *Jerky nystagmus*: There is slow movement to one side, which is followed by a corrective fast movement to the opposite side. This type of nystagmus is named on the basis of the direction of the fast component. Jerky nystagmus occurs when the child looks laterally (Table 3.15).

2. Types of nystagmus according to the amplitude are as follows:

Type of nystagmus	Amplitude of nystagmus	
Fine	1 mm	5°
Medium	1–3 mm	5–15°
Coarse	>3 mm	>15°

3. Types of nystagmus depending on the direction of the movement of the eyes are as follows:
   (a) *Horizontal*: Oscillation is around the vertical axis. Pendular nystagmus is a type of horizontal nystagmus.
   (b) *Vertical*: Oscillation is around the horizontal axis. It is seen in brainstem dysfunction.
   (c) *Rotatory*: Oscillation is around the anteroposterior axis.
4. Types of nystagmus based on the position of the head or eyes are as follows:
   (a) *End point nystagmus*: There is a slight oscillating or nystagmoid movement with the fast component in the direction of the gaze. This condition is seen in normal children when they look at one corner of the eye. This is not a true nystagmus.

TABLE 3.15 Direction of Jerky Nystagmus in Various Conditions

Condition/Lesion	Direction of Nystagmus
Cerebellar lesions	Towards the same side of lesion
Labyrinthine lesions	Towards the opposite side of lesion
Brainstem lesions	Rotatory nystagmus
Spinal cord lesions	Vertical nystagmus

   (b) *Fixation nystagmus*: This condition is seen when the patient focuses upon some point. This type of nystagmus is seen in patients with ataxia telangiectasia.
   (c) *Positional nystagmus*: It occurs with the change in position of the head. It is seen in children with vestibular dysfunction or posterior fossa tumours.

Other Types

- *Optokinetic nystagmus* is normally seen in children looking at a moving train or a drum with alternate black and white strips. It is absent in parietal lobe lesions.
- *Wandering nystagmus* is seen in blind children as an irregular, oscillatory movement with marked amplitude. The rapid component is absent.
- *Rotatory nystagmus* is seen in children with labyrinthine disease or tumours in medulla oblongata.
- *To-and-fro nystagmus* is seen in children with congenital nystagmus or spasmus nutans.

Causes

Causes of nystagmus can be classified as follows:

1. Physiological
   (a) Optokinetic nystagmus
   (b) Labyrinthine or vestibular nystagmus
2. Pathological
   (a) Congenital—congenital nystagmus presents at birth or within the first week of life. There is a positive family history. No other neurological abnormalities are usually seen
   (b) Acquired
      - Neurologic—lesions in the pons, medulla oblongata or cerebellum; tumours of posterior fossa; drugs—hydantoin overdosage, chronic barbiturate intoxication, benzodiazepines and phenothiazines
      - Vestibular—labyrinthine or vestibular nerve lesions
      - Ocular causes—blindness, visual disturbances, cataract, retrolental fibroplasias, astigmatism, weakness of extraocular muscles (gaze paretic nystagmus)

Grading

Nystagmus is graded according to the direction of the fast component.

Grade	Direction of nystagmus
1	Fast component of nystagmus is to the same side to which the child looks
2	Nystagmus occurs when the child looks straight
3	Fast component of nystagmus is to the opposite side to which the child looks

Other Eye Movements

1. *See–saw movements*: One eye moves up while the other eye moves down. This condition is seen in children with pontine lesion, cerebellar lesion and suprasellar tumours in the third ventricular region.
2. *Skew deviation*: One eyeball is maintained above the other. This condition occurs in posterior fossa lesions (brainstem and cerebellum) of CNS.
3. *Decreased movement of medial rectus on one side while attempting for lateral caze*: This condition arises due to internal ophthalmoplegia occurring in lesions of medial longitudinal fasciculus.
4. *Opsoclonus*: This movement is seen in children with neural crest tumours, especially neuroblastoma. It is characterised by rapid, chaotic, irregular jerky movements of the eyes in all directions. It is also known as dancing eyes.

Doll's Eye Phenomenon

Doll's eye movement is useful in young babies in the first 10 days of life and in comatosed patients who cannot cooperate. It is also known as *oculocephalic reflex*. With the baby lying supine, the head is turned quickly to one side. Look for the movements of the eyeball. The baby's eyes lag behind. Now, quickly turn the head to the other side and watch the movement of the eyeballs. Now move the head up and down and watch for the vertical movement of the eyeballs. Absence of Doll's eye movement is seen in children with transtentorial herniation or increased intracranial pressure.

Conjunctiva

Examination of the conjunctiva reveals relevant findings about various ocular as well as systemic conditions. Some of the important conjunctival findings in ocular conditions include the following:

- Phlyctenular keratoconjunctivitis is characterised by pinhead-sized yellowish or greyish white conical lesions accompanied by injection of the surrounding conjunctival vessels. The phlyctena usually occurs on the bulbar conjunctiva, cornea or limbus.
- Pinguecula is a slightly elevated, yellowish, wedge-shaped, benign lesion that extends from the inner canthus.

Some of the important conjunctival findings in systemic conditions are as follows:

- Pallor in anaemia
- Bitot's spots and xerosis (dryness) in vitamin A deficiency
- Bulbar conjunctival telangiectasia in ataxia telangiectasia (Fig. 3.12)
- Petechiae of the conjunctiva in infective endocarditis (due to embolic phenomenon)
- Subconjunctival haemorrhage in cases with violent cough such as whooping cough

Sclera

Examination of sclera can indicate many systemic disorders. The colour of sclera is noted. For instance,



FIGURE 3.12 Ataxia telangiectasia (Louis–Bar syndrome). Telangiectasia over the bulbar conjunctiva.

yellowish discolouration of sclera (icterus) is seen in jaundice. Colour is usually bluish in infants and young children. Similarly, blue sclera is seen in children with the following disorders:

- Diamond–Blackfan syndrome
- Ehlers–Danlos syndrome
- Hallerman–Streiff syndrome
- Iron deficiency anaemia
- Infantile glaucoma
- Marfan's syndrome
- Osteogenesis imperfecta

Cornea

Corneal diameter in a normal newborn is about 9–10 cm. It reaches the adult size of 12 mm by about 6–12 months.

Size and curvature of the cornea should be noted. Variations in size of cornea are as given below:

- *Microcornea:* An adult cornea of less than 10 mm in diameter is called microcornea.
- *Macrocornea:* If the adult cornea is more than 13 mm in diameter, it is called macrocornea.
- *Megalocornea or macrophthalmia:* It refers to an increase in both the corneal diameter and the anterior chamber depth. It is also associated with small pupils, tremulous iris and subluxated lens.

Corneal Clouding

Corneal clouding is seen in the following conditions:

1. Mucopolysaccharidosis
   - Hurler's syndrome
   - Morquio's syndrome
   - Scheie syndrome
   - Hurler–Scheie syndrome
   - Maroteaux–Lamy syndrome
   - Beta-glucuronidase deficiency (MPS VII)
2. Lysosomal syndromes
   - GM1 gangliosidosis and mannosidosis
   - Mucolipidosis
   - Tyrosinaemia

Keratitis

Keratitis refers to an inflammation of the cornea. It may be superficial or deep. It is often associated with circumcorneal injection. Causes of keratitis are as follows:

- Exposure keratitis as in paralysis of trigeminal nerve, lagophthalmos and defective closure of eyes during sleep
- Infections such as trachoma, congenital syphilis, tuberculosis and viral infections such as herpes simplex

Interstitial keratitis: Hazy cornea is seen in children with interstitial keratitis where the stroma of the cornea is affected. It is associated with infections or allergy.

Corneal Opacities

Corneal opacities can be caused by trauma or keratitis. Depending on the density, the opacity can be of the following types:

- Nebula—small cloudy opacities
- Macula—intermediate-density opacities
- Leucoma—large dense white opacities

Corneal Ulceration

Corneal ulceration is local necrosis of superficial corneal tissue associated with epithelial discontinuity. It is associated with intense pain, photophobia, lacrimation and blepharospasm. It is seen in patients with bacterial and fungal infections, vitamin A deficiency, herpes virus infection, etc.

Kayser–Fleischer Ring

Kayser–Fleischer ring is a golden- or greyish-brown ring located at the limbus of the cornea. It may be unilateral or bilateral and complete or incomplete. It is usually associated with the following diseases:

- Wilson's disease
- Familial cholestatic syndromes
- Chronic active hepatitis with cirrhosis

In Wilson's disease, pigmentary deposits are present, which are more prominent at the '12' and 6 o'clock positions. The Kayser–Fleischer rings are always present in patients with neurological findings but may be absent in patients with hepatic disease only.

Other Corneal Findings

- Corneal hypaesthesia: This condition refers to

the absence of corneal reflex. It is seen in cases with familial dysautonomia.
- Corneal xerosis: This condition refers to dryness of cornea. It is seen in cases with vitamin A deficiency.
- Corneal arcus: This condition is seen in children with hyperlipidaemia.

Iris

Table 3.16 lists the findings that should be looked for during the examination of iris.

Pupil

Examination of pupil yields information about a lot of ocular as well as neurological disorders. The examiner should assess the pupils of both eyes for the following parameters:

TABLE 3.16 Findings on Examination of Iris

Condition	Clinical Findings	Associated Conditions
Iridodonesis	Iris moves due to absence or dislocation of lens	Marfan's syndrome Homocystinuria
Aniridia	Absence of the entire iris	Wilm's tumour Neoplasms of the adrenal cortex and liver
Iris coloboma	Absence of part of the iris	Trisomy 13 CHARGE syndrome
Heterochromia	One blue and other brown eye	Normal variant Waardenburg syndrome
	Ipsilateral eye remaining blue	Horner's syndrome
	Iris on the involved side may be lighter	Cervical or mediastinal neuroblastoma
Lisch nodules	Yellow brown or non-pigmented, elevated, dome-shaped nodules in the iris	Neurofibromatosis type I
Brush field spots	Whitish speckling of iris (salt and pepper speckling)	Down's syndrome Cerebrohepatorenal syndrome Normal children
Stellate pattern	Lacy stellate pattern and blue irises	William's syndrome

- Size
- Shape
- Irregularity
- Difference in size
- Reaction to light
- Response to accommodation

Pupils start reacting to light from 31 weeks of gestation onwards. The normal pupillary diameter is 3–4 mm at birth. The size is usually equal in both eyes. Inequality in the size of both the pupils is called anisocoria. Anisocoria up to 1–2 mm may be considered normal if the difference remains the same in light and darkness.

A normal pupil reacts to light and accommodation by constricting. Persistent constriction without a light stimulus is abnormal. Causes of *constricted pupil* include the following:

- Argyll–Robertson pupil (due to pretectal lesion in ciliary ganglion)
- Barbiturate poisoning
- Brainstem lesions—pontine haemorrhage
- CNS disease irritating the third cranial nerve
- Coma due to metabolic causes
- Drugs—instillation of pilocarpine drops into the eyes and neostigmine overdose
- Encephalitis
- Floaters
- Geriatric age
- Horner's syndrome—sympathetic chain lesion
- Iritis
- Insecticide poisoning—organophosphorus poisoning
- Opium poisoning

Pupils will be constricted in bright light and in children with light-coloured eyes.

Causes of *dilated pupils* include the following:

1. Unilateral
   - Familial dysautonomia (Riley–Day syndrome)
   - Foster–Kennedy syndrome (a frontal lobe tumour; it compresses the optic nerve on one side. it is associated with papilloedema on the other side)
   - Holmes–Adie pupil is a tonic pupil. The size is usually larger but can be smaller than normal. There is sluggish or absent reaction to light.

The reaction to accommodation is better as compared to reaction to light. The abnormality is unilateral, resulting in unequal pupils. It reacts better to weak cholinergic drugs such as pilocarpine instilled into the conjunctival sac. After mydriatic instillation, there will be no reaction to light or accommodation

2. Bilateral
   - Atropine or belladonna poisoning
   - Brainstem compression—brain anoxia/ischaemia/death
   - Blindness due to lesions in the retina or optic nerve (optic nerve atrophy)
   - Cranial nerve palsy—oculomotor palsy
   - Drugs—barbiturate poisoning and glutethimide poisoning
   - Eye drops—mydriatic eye drops
   - Familial dysautonomia—tonic pupil (Riley–Day syndrome)
   - Glaucoma—advanced glaucoma
   - Injury—head injury or transtentorial herniation of temporal lobe causing compression or traction of oculomotor nerve
   - Increased intracranial tension
   - Jimson weed poisoning—dhatura poisoning

In children with dark eyes, pupils will be dilated in dim light. Table 3.17 describes some conditions with abnormal pupillary reactions.

TABLE 3.17 Conditions with Abnormal Pupillary Reactions

Condition	Clinical Features
Argyll–Robertson pupil	Small, irregular, unequal pupils Absent light reflex Accommodation reflex present Depigmented iris Incomplete response to mydriatics
Horner's syndrome	Constricted pupils Enophthalmos Drooping of the eyelid (ptosis) Mydriasis Heterochromia (different colour of iris)
Holmes–Adie pupil	Unilateral dilated pupil—vary in size from small to large Sluggish or absent reaction to light Accommodation—convergence reflex for near vision occurs slowly
Marcus–Gunn pupil	Relative afferent pupillary defect Seen in optic nerve injury Swinging flash light positive
Hippus	Rhythmic contraction and dilatation of the pupil spontaneously or in reaction to light May be seen in normal individuals or in patients with retrobulbar neuritis

Leukocoria (White Pupil)

Leukocoria is also known as white eye reflex or cat's eye reflex. This condition is characterised by a grey-white appearance of the pupil on examination of the eyes. It is observed in the following conditions:

- Mature cataract
- Persistent hyperplastic primary vitreous
- Retrolental fibroplasia
- Endophthalmitis
- Organised vitreous haemorrhage
- Extensive retinal detachment
- Retinoblastoma
- Retinopathy of prematurity
- Retinal dysplasia
- Uveitis from toxoplasmosis, cytomegalovirus or herpes
- Congenital detachment of dysplastic retina

Lens

The examiner should look for dislocation of lens and cataract (Fig. 3.13).

Dislocation of Lens

Dislocation of lens is associated with the following conditions:

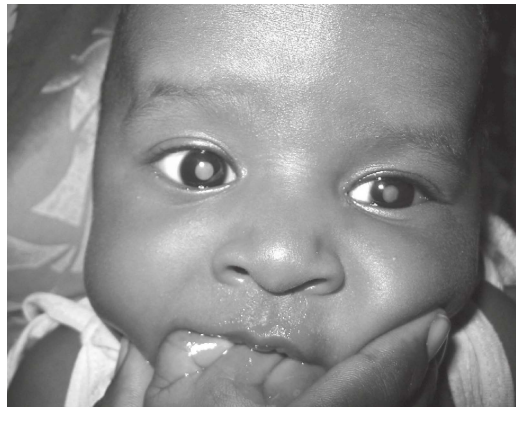


FIGURE 3.13 Cataract.

- Marfan's syndrome
- Homocystinuria

Cataract

Fifty per cent of the cataracts seen in the infants are of unknown aetiology. In addition to the idiopathic and hereditary factors, the causes of cataract include the following:

1. Intrauterine infections cause central or nuclear cataracts
   - Toxoplasmosis
   - Cytomegalovirus (CMV)
   - Rubella—in rubella, development of lens is inhibited at an early stage so that central nucleus remains opaque (nuclear cataract)
   - Syphilis
2. Metabolic causes
   - Galactosaemia (cortical opacity)
   - Diabetes mellitus (snow flame opacities in posterior subcapsular region)
   - Wilson's disease (sunflower cataract)
   - Hypocalcaemic tetany (lamellar cataract)
   - Phenylketonuria
   - Homocystinuria
   - Aspartyl glycosaminuria
   - Galactokinase deficiency
   - Homocystinuria
   - Peroxisomal disorders
   - Refsum's syndrome
3. Storage disorders
   - Mucopolysaccharidosis
   - Mannosidosis
   - Mucolipidosis
4. Endocrine disorders
   - Cretinism (punctate subcapsular cataract)
   - Hypoparathyroidism
5. Chromosomal causes
   - Down's syndrome
   - Trisomy 13
   - Trisomy 18
   - Turner's syndrome
6. Secondary to intraocular processes
   - Retrolental fibroplasia
   - Retinitis pigmentosa
   - Retinal detachment
   - Uveitis
7. Physical agents
   - Trauma
   - Radiation
8. Cataract of prematurity—opacities occur in Y-shaped distribution, which disappear spontaneously
9. Drugs
   - Corticosteroid (long-term use of high dose of steroids leads to posterior subcapsular cataract)
   - Chlorpromazine
   - Hypovitaminosis D
   - Hypervitaminosis D
   - Tetracycline
10. Miscellaneous
    - Alport's syndrome
    - Cockayne syndrome
    - Conradi disease (chondrodysplasia punctata)
    - Diamond–Blackfan syndrome
    - Hallermann–Streiff syndrome
    - Incontinentia pigmenti
    - Kartagener syndrome
    - Lowe's syndrome (cerebrohepatorenal syndrome)
    - Mandibulofacial dysostosis
    - Marfan's syndrome
    - Myotonic dystrophy
    - Osteopetrosis
    - Smith–Lemli–Opitz syndrome

Vitreous

Floaters are opaque substances floating in the vitreous. Children can see the floaters, but they cannot focus on them due to constant motion of the vitreous. When a child looks at a plain background such as white paper or blue clear sky, these become evident.

The floaters may vary in size, number and shape. They may be seen as spots, dots, wavy lines, cloudy or other forms. They are seen in the following conditions:

- Normal eyes

- Myopia
- Vitreous detachment (more common in old age)
- Retinal disorders

Fundoscopic Examination

Fundoscopic examination is an examination of the retina. It is best done through a dilated pupil, with the patient's gaze fixed on a distant object. Children above 4 years of age usually comply when asked to fix the gaze on a coloured object. The examiner should look for normal and abnormal patterns in the optic nerve head, macula and peripheral retina.

Some relevant fundoscopic findings include the following:

1. Chorioretinitis
2. Papilloedema (optic disc oedema):
   - Unilateral papilloedema is seen in patients with tumours and Foster–Kennedy syndrome
   - Bilateral papilloedema is associated with pseudotumour cerebri
   - Pseudopapilloedema
3. Cherry red spot—it is characterised by a red spot at the centre of the macula, surrounded by a greyish-white ring. The central red area is normal choroidal vasculature, and the ring is formed due to accumulation of abnormal substances in the retinal ganglion cells or ganglion cell oedema. Causes of cherry red spot include the following:
   - Sialidosis I and II
   - Infantile Gaucher disease or
   - GM1 gangliosidosis (Tay–Sachs disease)
   - GM2 gangliosidosis (Sandhoff's disease)
   - Niemann–Pick disease
   - Metachromatic leukodystrophy
   - Mucolipidosis I
4. Retinal haemorrhages are seen in patients with bleeding disorders, leukaemia, diabetic retinopathy, hypertensive retinopathy and central retinal vein occlusion. They can be superficial, deep or subhyaloid:
   - Superficial haemorrhages are elongated and flame shaped
   - Deep haemorrhages are rounded (dot or blot)
   - Subhyaloid haemorrhages are large and have horizontal upper border (boat shaped)
5. Pallor or tortuosity of vessels
   - The fundus appears pale in severe anaemia
   - The retinal vessels are dark, tortuous and dilated in polycythaemia and leukaemia
   - In leukaemia, retinal vessels are tortuous and dilated. Retinal haemorrhages may be seen
6. Retinal pigmentary changes
   - Congenital pigmentation of the retina—grey or greyish black spots
   - Retinitis pigmentosa (Table 3.18)
   - Peroxisomal disorders such as Zellweger (cerebrohepatorenal) syndrome

TABLE 3.18 Retinitis Pigmentosa

Characteristics	Description
Retinal changes	Degeneration, atrophy and pigmentation of retina associated with waxy pallor of optic disc Jet black spots on the affected part of retina
Prominent clinical features	Night blindness Progressive constriction of the visual fields
Associated syndromes	Laurence–Moon–Biedl syndrome Usher's syndrome Cockayne syndrome Kearns–Sayre syndrome Refsum's syndrome Bassen–Kornzweig syndrome

NOSE

Nose is situated in the dangerous area of the face. Any infection of this area predisposes to cavernous sinus thrombosis. Also, the appearance of the nose depends on the development of the base of skull. The appearance of the nose will give clue to a number of disorders (Table 3.19).

Nasal Bridge

Flat nasal bridge is seen in the following conditions:

- Carpenter's syndrome
- William's syndrome

TABLE 3.19 Appearance of Nose in Various Disorders

Appearance of Nose	Disease
Broad and long nose	Fragile X syndrome
Narrow nose with hypoplastic alae nasi	Edward's syndrome
Upturned nose	Marshall–Smith syndrome
Beaking of nose	Osteogenesis imperfecta, craniofacial dysostosis and Rubinstein–Taybi syndrome
Broad nasal tip	Coffin–Siris syndrome (onychodysplasia syndrome)

- Coffin–Siris syndrome (onychodysplasia syndrome)

Depressed nasal bridge is seen in the following conditions:

- Anaemia—thalassaemia major and osteopetrosis
- Bone disorders—skeletal dysplasia
- Chondrodystrophy
- Conradi syndrome
- Down's syndrome
- Ectodermal dysplasia
- Familial (in normal children)
- Genetic disorders—Larsen's syndrome
- Hurler's syndrome—mucopolysaccharidosis
- Hypothyroidism or cretinism
- Infections—congenital syphilis

Saddle nose is seen in patients with congenital syphilis and Laron syndrome.

Nostrils

Nostrils are anteverted in the following conditions:

- William's syndrome
- Aarskog syndrome
- Smith–Lemli–Opitz syndrome

Nasal polyps are seen in cystic fibrosis.

Philtrum

Philtrum is the area between the columella of the nose and the upper lip. This part develops from the frontonasal process. The superficial part is formed by the fusion of the maxillary process.

It is short in the following conditions:

- Di George syndrome
- Orofaciodigital syndrome

It is long in the following conditions:

- Aarskog syndrome
- Foetal alcohol syndrome
- Foetal hydantoin syndrome
- William's syndrome
- Cornelia de Lange syndrome

It is elongated in patients with Weaver–Smith syndrome.

EARS

Ears should be examined carefully, as the type of deformities will give clue to many clinical conditions. Important findings to be looked for while examining the ears include the following:

1. Preauricular sinuses are remnants of the first branchial cleft. They may get infected and should be excised
2. Partial or complete absence of pinna as in Goldenhar's syndrome (Fig. 3.14)
3. Deformed pinna. Ear lobule is abnormal in Treacher–Collins syndrome and Seckel syndrome
4. Preauricular skin tags. Small skin tags may be present in front of the ear as in Goldenhar's syndrome
5. Prominent ears are seen in Fragile X syndrome
6. Microtia (small ears) is seen in Treacher–Collins syndrome and Goldenhar's syndrome
7. Low set ears (Fig. 3.15) are seen in the following cases
   - Apert's syndrome
   - Bird-headed (Seckel's) dwarfism
   - Cri-du-chat syndrome
   - Carpenter's syndrome
   - Cornelia de Lange syndrome
   - Down's syndrome
   - Elfin facies (William's syndrome)
   - Foetal hydantoin syndrome
   - Leopard syndrome
   - Mucopolysaccharidosis
   - Noonan's syndrome



(a)



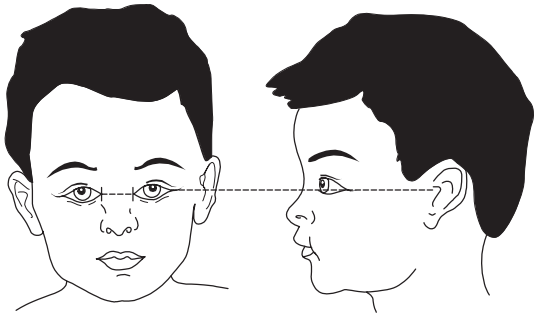
(b)

FIGURE 3.14 Goldenhar's syndrome. (a) Absence of pinna with micrognathia. (b) Preauricular skin tag.

- Pierre–Robin syndrome
- Potter facies—renal agenesis
- Smith–Lemli–Opitz syndrome
- Treacher–Collins syndrome
- Turner's syndrome
- Trisomy 13 and 18

MOUTH

During the examination of the mouth, the clinician should note the size of the mouth and look for any abnormality in the perioral region, lips and buccal mucosa.



(a) (b)

FIGURE 3.15 Method to look for low set ears: With the patient standing straight, an imaginary line is drawn from the outer canthus, parallel to the floor. (a) Normally, this line crosses the ear in such a way that about one-third of the pinna lies above this imaginary line. (b) When less than one-third of the pinna lies above this line, the patient is said to have low set ears.

Size

Normally, the outer edge of the mouth lies on a perpendicular line dropped from the centre of the either pupil, with the eyes looking straight. If the outer edge of the mouth falls within the lines, the child is said to have *microstomia*. This condition is seen in children with whistling face syndrome. In *macrostomia*, the outer edge of the mouth falls outside the line described above. It is seen in infants of diabetic mothers.

Appearance

Fish-like mouth is seen in the following cases:

- Treacher–Collins syndrome
- William's syndrome
- Oculoauriculovertebral dysplasia
- Congenital myotonic dystrophy
- Idiopathic hypercalcaemia

Floor

Ranula is a retention cyst of the sublingual glands. It is seen on either side of the frenulum. It is bluish and translucent in appearance.

Perioral Region

The examiner should look for the following syndromes:

- Angular stomatitis—maceration, fissuring and proliferative growth at the angle of mouth is seen in vitamin B_2 or riboflavin deficiency.
- Cheilitis—lips are dry, cracked and may be crusted and ulcerated in vitamin B_2 or riboflavin deficiency.
- Telangiectasia—localised dilatation of small blood vessels is seen in ataxia telangiectasia.
- Rhagades—white scars at the angles of the mouth are seen in congenital syphilis.

Lips

Examination of lips will give clue to various clinical conditions.

Appearance	Condition
Blue lips	Cyanosis
Parched lips	Severe dehydration
Cheilosis (cracks and fissures at the mucocutaneous junction of the lip)	Riboflavin deficiency Iron deficiency Nicotinic acid deficiency Exposure to cold

Buccal Mucosa

Buccal mucosa is the inner surface of the cheeks. The examiner should look for any change in mucosal colour and any abnormal pigmentation inside the mouth. Examine on both sides. Swelling and ulcers should be palpated.

Some relevant findings include the following:

- Koplik's spots are small papules on faint erythematous base on the buccal mucosa. They are bright red or rose-coloured spots with whitish centre seen during the prodromal stage of measles. They are seen near the opening of the parotid duct opposite to the first lower molar teeth in patients with measles.
- Aphthous ulcers (Canker sores) are painful recurrent oral ulcers seen in the mouth—ventral surface of the tongue, cheeks, lips, soft palate and base of gums. They may be single or multiple. The ulcers may be less than 0.5 cm in diameter, with depressed centre and erythematous periphery. The aetiology is not known.
- Thrush is a fungal infection usually caused by Candida albicans. It appears as a white patch in the mouth.
- Pigmentation—brown or blue-black pigmentation of the buccal mucosa due to increased melanin is seen in Addison's disease and Peutz–Jeghers syndrome.
- Ulcers may be seen in children with leukaemia.
- Chicken pox lesions (enanthem) are present as pleomorphic rashes with central umbilications.
- Traumatic ulcers of the buccal mucosa are seen in children with sharp teeth. The sharpness should be blunted in order to prevent injury to the buccal mucosa.

Teeth and Gums

Examination of teeth and gums gives clue to a lot of medical conditions. It reflects the oral hygiene and many systemic disorders. Any defect in the skeletal maturation may cause delayed dental development.

Teeth

Relevant findings in teeth examination include the following:

1. Colour of the teeth

Colour	Conditions
Red teeth (erythrodontia)	Erythropoietic porphyria
Bluish-grey and brown staining	Use of tetracycline in children below 8 years of age or in mothers during the in utero period
Green	Neonatal hyperbilirubinaemia
Chalky white	Fluorosis
Brownish	Amelogenesis imperfecta—a disorder of tooth development. It occurs due to malfunction of ameloblasts that form enamel
Black	Iron tablets

2. Malocclusion is an improper dental alignment where the upper teeth do not align properly with the lower teeth. Thumb sucking and injury predispose to this condition.
3. Teeth are absent in the following conditions:
   - Ectodermal dysplasia
   - Cleidocranial dysostosis
4. Natal teeth—if teeth are present at birth, they are called natal teeth. Lower incisors may be present in some normal babies. They do not interfere with feeding. As they are mobile and do not usually cause injury to the breast while suckling, they need not be removed. They fall spontaneously in few days. If they are very loose and there is risk of aspiration, they may be removed any time.
5. Neonatal teeth—if teeth erupt in the first month of life, they are called neonatal teeth. They are seen in the following conditions:
   - Ellis–van Creveld syndrome
   - Pierre–Robin syndrome
6. Caries teeth—these can predispose to infective endocarditis in children with congenital heart defects.
7. Hutchinson's teeth—peg-shaped upper permanent central incisors are seen in congenital syphilis.
8. Mulberry molars—multiple poorly developed cusps are usually seen in the first molars in congenital syphilis.
9. Enamel defects are common in hypocalcaemic rickets.
10. Pulp defects are common in hypophosphataemic rickets.
11. Delayed dentition occurs in the following conditions:
    - Hypothyroidism
    - Down's syndrome
    - PEM
    - Rickets
    - Hypopituitarism

Gums

The clinician should look for these findings during the examination of the gums:

1. Gum hypertrophy occurs due to the following causes:
   - Drug induced—phenytoin and nifedipine
   - Scurvy
   - Acute myelomonocytic leukaemia (AML-M4) and acute monocytic leukaemia (AML-M5)
   - Amyloidosis
   - Hunter's syndrome
   - Hurler's syndrome
   - Epulis—benign neoplasm or hyperplasia of gums
2. Blue line (Burton's line) on the gums occurs in lead poisoning
3. Swollen, red and spongy gums that bleed easily are seen in scurvy
4. Other causes of gum bleeding—acute lymphoblastic leukaemia and thrombocytopenia
5. Hyperpigmentation—Addison's disease and haemochromatosis

Tongue

The tongue is associated with the following functions:

- *Taste sensation*: The tongue is supplied by the chorda tympanic branch of facial nerve (which carries taste sensations from anterior two-thirds of the tongue) and the glossopharyngeal nerve (which carries taste sensations from posterior one-third of the tongue).
- *Swallowing*: The tongue pushes the bolus towards the oropharynx during the oral phase of swallowing.
- *Chewing*: The tongue helps in chewing by pushing the food in between the teeth.
- *Speech*: The tongue is essential in the production of various sounds.

The clinician should note the size, colour, appearance and movement of the tongue.

Glossoptosis is the posterior positioning of the tongue. It is seen in the following conditions:

- Hypoplasia of mandible
- Small mouth cavity as in Pierre–Robin syndrome and Down's syndrome

Protrusion of tongue may occur due to an enlargement of the tongue, as seen in the following

conditions:

- Cretinism
- Myxoedema
- Amyloidosis

Size

The growth of the tongue follows the pattern of neural growth. Hence, the growth is more rapid in the latter part of pregnancy. The size of the tongue, therefore, appears large at birth. A normal-sized tongue is never seen protruding out of a normal-sized mouth. Macroglossia (large tongue, Fig. 3.16) occurs in the following cases:

- Lymphangioma or haemangioma of tongue
- Mucopolysaccharidosis
- Hypothyroidism—cretinism and myxoedema
- Glycogen storage disorders—Von Gierke's disease and Pompe's disease
- Amyloidosis
- Acromegaly
- Down's syndrome (relative macroglossia)—the tongue protrusion in Down's syndrome is due to a small mouth rather than a large tongue (Fig. 3.1b)

Microglossia (small tongue) occurs in the following conditions:

- Spastic paralysis in pseudobulbar palsy (cerebral diplegia)—atrophy of tongue is seen
- XII cranial nerve palsy—wasting of tongue is seen in bulbar palsy, motor neuron disease and lower motor neuron lesions of hypoglossal nerve

Colour

The normal colour of the tongue is red due to presence of fungiform papillae, which are rich in blood vessels. The colour of the tongue may vary in the following conditions:

- Pale tongue is seen in anaemia.
- White strawberry tongue is seen when the red inflamed fungiform papillae are surrounded by white-coated background. It is produced by the smaller filiform papillae. It is seen in children with second to fifth day of scarlet fever, measles and other febrile illnesses.
- Magenta-red tongue is seen in riboflavin deficiency.
- Bright red strawberry tongue (Fig. 3.17) or raspberry tongue with prominent inflamed red fungiform papillae is seen in scarlet fever. The white coating and filiform papillae shed after 6–7 days of scarlet fever, leaving a red background.
- Blue tongue is seen in cyanotic heart diseases, methaemoglobinaemia and sulphaemoglobinaemia.
- Black tongue is seen after ingestion of bismuth, liquorice and charcoal.
- Black hairy tongue is seen in fungal infections.
- Yellow tongue is seen in jaundice.
- Bluish red tongue is seen in polycythaemia.
- Red, swollen beefy tongue is seen in pellagra and vitamin B_{12} deficiency.
- Smooth, red tongue is seen in pernicious anaemia.

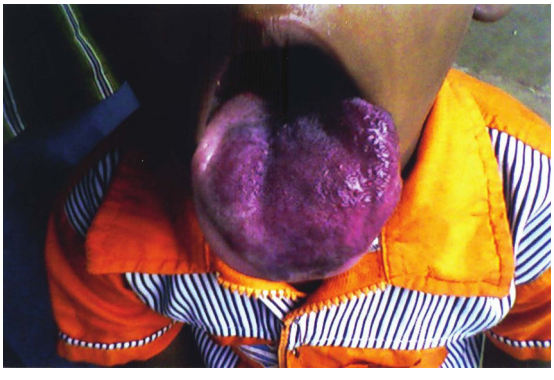


FIGURE 3.16 Macroglossia.



FIGURE 3.17 Bright red strawberry tongue.

- White patches on the tongue are seen in Candida infection.

Appearance

The normal tongue is red and moist due to rich blood supply and secretion of mucous and serous fluids. The circumvallate papillae are arranged in a form of 'V' at the posterior part of the tongue. At the apex of this angle, a small invagination is seen, which is known as foramen caecum.

Some abnormal appearances of tongue include the following:

- Geographical tongue (migratory glossitis) is a benign condition characterised by irregularly shaped red, map-like smooth patches on the otherwise normal tongue. This condition arises due to rapid loss and regrowth of filiform papillae. The patches may be single or multiple, discrete or confluent. This condition will persist for few weeks and then regress spontaneously and may reappear again. It is not significant and may be seen in normal children.
- Wasting of tongue is seen in XII cranial nerve palsy.
- Coating of the tongue is seen in typhoid fever.
- Dry tongue—the moistness of the tongue depends on the state of hydration. The tongue is usually dry in dehydration.
- Generalised atrophy of the papillae—this condition occurs in vitamin B_{12} deficiencies and gives the tongue a smooth or bald appearance.
- Fissuring of the tongue (scrotal tongue, plicated tongue and lingua plicata)—it refers to a painless groove on the dorsal surface of the tongue. This condition is associated with Down's syndrome.
- Raw beefy tongue—red, swollen and painful tongue is seen in pellagra and vitamin B_{12} deficiency.
- Strawberry tongue is seen in scarlet fever. There will be hypertrophy of fungiform papillae.
- Bald tongue occurs due to atrophy of papillae. It is seen in conditions such as pellagra, pernicious anaemia, iron deficiency anaemia and tropical sprue.
- Black hairy tongue is a result of elongation of filiform papillae, as seen in patients with prolonged antibiotic use.
- Spastic tongue is seen in pseudobulbar palsy.
- Flaccid tongue is seen in hypoglossal nerve palsy.

Frenulum

- Frenal ulcers occur due to violent cough such as whooping cough.
- Tongue tie is a condition where the tongue is attached to the floor of the mouth by frenulum (Fig. 3.18). The mobility of the tongue is restricted. Pronunciation of words is difficult if it is not released. If the frenulum is thin and is not interfering with the movements of the tongue, no intervention is needed. If the frenulum is thick, producing a notch at the tip of the tongue, it has to be released by the age of 3 months.

Movements

To assess the movement of the tongue, the examiner should ask the child to protrude the tongue out and move it from side to side. Abnormal findings to be looked for include the following:

1. Inability to protrude the tongue is seen in tongue-tie.
2. Inability to move the tongue is seen in bilateral XII cranial nerve palsy.
3. Deviation of tongue is seen in unilateral XII cranial nerve palsy and hemiplegia. In unilateral XII cranial nerve palsy, the tongue deviation is to the same side, but in hemiplegia the tongue is deviated towards the paralysed side.
4. Abnormal movements of the tongue:

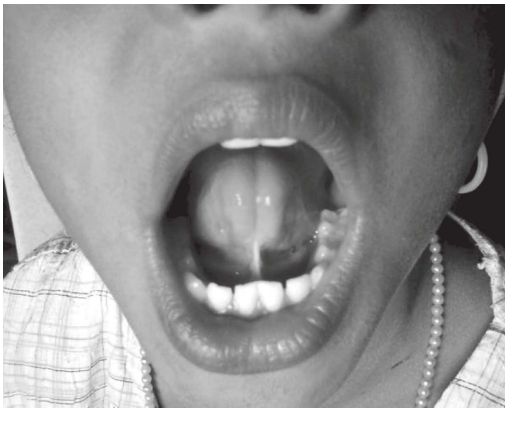


FIGURE 3.18 Tongue tie.

- When the child is asked to protrude the tongue, he or she is unable to protrude it in a sustained manner. This condition is known as *darting tongue* or *Jack-in-the-box tongue* and is seen in children with chorea.
- The tongue is protruded out and retracted immediately. This condition is known as *lizard tongue* and is seen in children with chorea.
- Repeated chewing movements of the tongue are seen in athetosis.
- Irregular movements are seen in extrapyramidal lesions.
- Tremors are seen in thyrotoxicosis.
- Fasciculation of the tongue is contraction of a motor unit. It occurs when the cranial nerve nuclei of the XII cranial nerve is affected. It is seen in motor neuron disease.
- Fibrillation is contraction of individual muscle fibres. It is diagnosed using an electromyogram. It is seen in children with complete denervation of any of the muscles of the tongue.

Swelling over the Tongue

- Thyroglossal cyst at the base of the tongue
- Ectopic lingual thyroid

Palate

Palate is the upper part of the mouth. The child is asked to open the mouth widely, and the palate is examined from the upper incisors to the uvula.

High-Arched Palate

To detect a high-arched palate, the clinician should ask the child to stand straight, look forward and open the mouth. Normally, the posterior part of the palate is easily visualised. In patients with high-arched palate, one cannot visualise the posterior part of the palate (Fig. 3.19). Conditions associated with high-arched palate are as follows:

- Cornelia de Lange syndrome
- Down's syndrome
- Marfan's syndrome
- Turner's syndrome

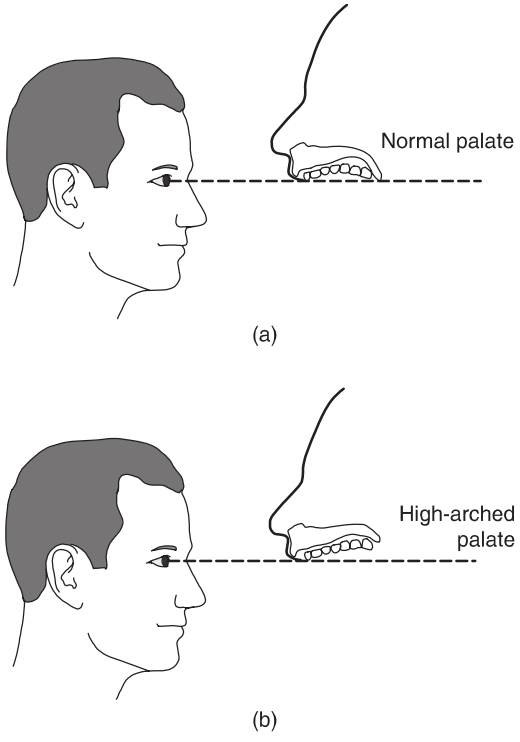


FIGURE 3.19 Look at the level of incisors—with patient looking straight. (a) In normal children, soft palate/uvula is visible. (b) In children with high-arched palate, uvula is not visible.

Cleft Palate

The clinician should inspect both the hard and the soft palates and note if the cleft is partial or total. Often cleft lip and palate are seen together. Conditions associated with cleft palate are as follows:

- Apert's syndrome
- Cornelia de Lange syndrome
- Diastrophic dysplasia
- Drugs—diphenylhydantoin
- Faciomandibulo dysostosis
- Pierre–Robin syndrome
- Velocardiofacial syndrome

Cleft lip and palate are seen together in the following conditions:

- Frontonasal dysplasia
- Meckel–Gruber syndrome
- Orofaciodigital syndrome

- Short rib polydactyly syndrome
- Trisomy 13
- Drugs—androgens, barbiturates and diazepam

The position of the uvula should also be noted.

Movement of Soft Palate and Gag Reflex

To look for the movement of the soft palate, ask the child to say 'Ah' and note the rise of the soft palate. To elicit the gag reflex, touch the posterior pharyngeal wall with a wisp of cotton and note the response. Gag reflex is absent in IX and X cranial nerve palsies.

Ulcers and Vesicles

Vesicles confined to one side of the hard palate, which progress to painful ulcers, are seen in herpes zoster, affecting the maxillary division of the trigeminal nerve. Similar lesions are seen on the pharynx when the glossopharyngeal nerve is affected with herpes.

Jaw

Examine both the upper and the lower jaws. Ask the child to close the mouth. Observe if both upper and lower jaws close in approximation to each other. The mandible appears relatively small at birth. This grows forward and downwards in the early life. In the later infancy period, this appears more proportionate to the face.

Prognathia is a condition where the lower jaw protrudes the upper jaw. It is seen in the following cases:

- Chondrodystrophy
- Crouzon's disease
- Acromegaly in case of adults

Retrognathia is a condition where the upper jaw protrudes the lower jaw. Retrognathia is a posteriorly placed mandible. It may arise due to small mandible or a normal-sized posteriorly placed mandible.

Micrognathia is a condition where the size of the jaw is small (see Fig. 3.14). If the mandibular growth is affected, the upper and lower teeth will misalign. Also, the tongue will be pushed back. Often the tongue may press the palate predisposing to cleft palate. So if small mandible is noted, cleft palate should be carefully looked for. Micrognathia is seen in the following conditions:

- Cri-du-chat syndrome
- Foetal alcohol syndrome
- Pierre–Robin syndrome
- Rubinstein–Taybi syndrome
- Russell–Silver syndrome
- Treacher–Collins syndrome
- Trisomy 13 and 18
- Smith–Lemli–Opitz syndrome
- Zellweger syndrome

Macrognathia refers to an abnormally large jaw. It is seen in children with Sotos' syndrome.

Trismus is an inability to open the jaws. It may be associated with the following conditions:

- Brain tumours
- Drugs—phenothiazine toxicity
- Encephalitis
- Gaucher's disease (infantile form)
- Hypoparathyroidism (primary)
- Infections—tetanus
- Jaw tumours such as rhabdomyosarcoma
- Risus sardonicus—facial muscle spasm will give a fixed sardonic grin

THROAT

The throat of the child should be examined, as a source of infection may be present in the throat. A tongue depressor is used to press the tongue down and the following parts should be checked.

1. *Pharynx*: Pooling of saliva is seen in bulbar palsy. Also, look for gag reflex.
2. *Fauces*: It is an area in the lateral wall of the pharynx where the tonsils are situated. Erythema of fauces is seen in children with tonsillitis, pharyngitis, etc.
3. *Tonsils*: These should be examined for the following conditions. Tonsils may be enlarged even in normal children.
   - Tonsils are enlarged and erythematous in tonsillitis.
   - Petechiae are seen in diseases such as thrombocytopenia, rubella or streptococcal tonsillitis.
   - A white patch in the tonsillar area is seen in

children with diphtheria, candidiasis, streptococcal tonsillitis and agranulocytosis.

4. *Larynx*: It is examined by direct and indirect laryngoscopy. In infants and small children who cannot cooperate by opening the mouth, direct laryngoscopy is done.

NECK

Neck connects the head with the thorax. Arteries, veins and nerves are present here, and these lie in close approximation. Any condition affecting these makes the adjacent structures more vulnerable. A careful clinical examination should be done to avoid collateral harm to the patient. For example, both the carotids should not be palpated together, as this will result in decreased blood supply to brain and loss of consciousness. The neck should be examined for the following:

- Length of the neck
- Webbing of neck
- Swellings
- Sinuses
- Torticollis
- Neck rigidity
- Jugular venous pressure (JVP)
- Hepatojugular reflex
- Position of trachea
- Laxity of skin

Length

The neck usually appears short in infants. To check the length of the neck, the examiner should first measure the height or length of the child. Next, the distance between the external occipital protuberance and C_7 vertebra should be measured. In normal children, the overall height or length is 13 times the distance between the C_7 and occipital protuberance. If this ratio is 14 or more, it means that the patient has a short neck. Causes of short neck include the following:

- Cornelia de Lange syndrome
- Diamond–Blackfan syndrome
- Down's syndrome
- Hypothyroidism
- Klippel–Feil deformity
- Klinefelter's syndrome
- Meckel–Gruber syndrome
- Mucopolysaccharidosis
- Noonan's syndrome
- Platybasia
- Turner's syndrome

Causes of long neck include the following:

- Cornelia de Lange syndrome
- Marfan's syndrome
- Williams' syndrome

Swan neck appearance will be seen in children with myopathies.

Webbing

Webbing of the neck is seen in the following conditions:

- Diamond–Blackfan syndrome
- Meckel–Gruber syndrome
- Noonan's syndrome
- Turner's syndrome

Swellings

- Branchial cysts are seen along the course of the first and the second branchial clefts.
- Cystic hygroma is lymphangioma in the head and neck region, which appears early in life. These may present as unilocular or multicystic masses with thin, transparent walls. They are cystic, compressible and non-tender. They do not resolve spontaneously and should be resected completely (Fig. 3.20).
- Lymph nodes enlargement (lymphadenitis) occurs due to infection in the draining area, leukaemia and lymphomas.
- Thyroid gland enlargement (goitre) occurs in hypothyroidism.
- Thyroglossal cysts are situated in the midline of the neck. They may extend up to the base of the tongue. On moving the tongue, the swelling moves upwards. The cyst may contain mucinous material or, sometimes, thyroid tissue. The cyst should be excised surgically. Try to preserve the thyroid tissue. In a few cases, removal of the thyroid tissue in the cyst may result in hypothyroidism.



FIGURE 3.20 Cystic hygroma.

Sinuses

- Branchial sinuses are seen along the anterior border of sternocleidomastoid muscle. These sinuses are seen along the course of the first and the second branchial clefts due to improper closure of the branchial cleft in the embryonic life. They may drain into the skin or pharynx.
- Tuberculous nodes may rupture into the skin and form sinuses.

Torticollis

The child keeps the neck in such a position that the head is flexed to one side, with the chin pointing to the opposite side. It is seen in the following conditions:

1. Congenital
   (a) Sternomastoid tumour—this is a misnomer. Actually there is a bleeding in the muscle fibre probably during delivery, which is replaced by fibrous tissue. This gives rise to a swelling in the muscle. This is a benign condition
   (b) Muscular cause—absence of sternocleidomastoid muscle.
   (c) Skeletal causes
      - Congenital defect in odontoid process
      - Failure of fusion of odontoid process and the body of axis
      - Congenital vertebral anomaly such as hemivertebra

   (d) Ligamental cause—congenital absence of transverse ligament
2. Acquired
   (a) Infections
      - Quinsy—tonsils are inflamed and tender. The child keeps the head flexed to the affected side to minimise pain
      - Acute cervical lymphadenitis

   (b) Neurological causes:
      - Cerebellar tumours protruding through foramen magnum. When the head is flexed on the same side of protrusion, the protruding tumour does not press the brainstem or spinal cord. Hence, the child adopts this position
      - Syringomyelia
      - Lateral rectus palsy—abduction of the eyeball is not possible in these cases. If the child looks on the affected side, diplopia will be observed. To avoid this, the child will assume this position by turning the head towards the paralysed side

   (c) Functional cause: This condition disappears with sleep

Jugular Venous Pressure

JVP (refer Chapter 8) can be assessed by observing the jugular vein at the neck. The child is made to recline in bed at an angle of 45°, with his or her back and neck adequately supported. The child is asked to turn the neck to one side. A torch beam is directed tangentially across the neck. The upper level of pulsations in the jugular vein is seen. In normal children, the pulsations lie behind the sternum and cannot be seen. If the JVP is raised, the pulsations are seen in the neck.

Pulsations

Neck pulsations due to carotid artery flow become prominent in the presence of hyperdynamic circulation.

Dancing carotids are seen in aortic regurgitation.

Position of the Trachea

The trachea in a normal child is in the midline or slightly deviated to the right due to the presence of heart. In collapse lung, the trachea will be shifted to the ipsilateral side. In conditions such as pleural effusion, hydrothorax, pneumothorax and obstructive emphysema due to foreign body, the trachea is deviated to the contralateral side. In consolidation and thickening of pleura, there is no shift.

Laxity of Skin

Laxity of skin is seen in Ehlers–Danlos syndrome, Down's syndrome and pseudoxanthoma elasticum.

Examination of the Back of the Neck

1. Low posterior hairline—hairline usually lies at the level of C_4 in normal children. The low posterior hairline is seen in the following conditions:
   - Cornelia de Lange syndrome
   - Turner's syndrome
2. Lymph nodes: *See* page 82.

CHEST OR THORAX

The chest is the part in between the neck and the abdomen. This is a closed cage, with heart and lungs lying inside. Abnormal findings in chest include the following:

1. Absent pectoralis. Pectoralis major muscle is absent in Poland's syndrome.
2. Widely spaced nipples are said to be present if the internipple distance is more than 25% of the chest circumference. It is seen in the following conditions:
   - Meckel–Gruber syndrome
   - Noonan's syndrome
   - Turner's syndrome.
3. Polythelia (supernumerary nipples) are seen along the milk line. These are usually asymptomatic. However, these may be associated with cardiovascular or urinary abnormalities (Fig. 3.21).



FIGURE 3.21 Polythelia—accessory nipples.

4. Spider naevi consists of central artery with multiple dilated radiating vessels. The central artery is the feeder artery. This spider naevi is surrounded by erythematous flush. Pressing the central feeding artery results in blanching of all the dilated radiating vessels. It occurs due to vasodilatation caused by increased levels of oestrogens as happens in liver failure.
5. Chest asymmetry is seen in collapse or fibrosis of lung, foreign body obstruction on one side and scoliosis.
6. Chest deformities:
   - Pectus carinatum or pigeon chest refers to forward protrusion of sternum with straightening of the anterior ribs. It is seen in rickets.
   - Pectus excavatum refers to funnel-shaped depression of the lower end of sternum. It is seen in Marfan's syndrome, rickets and upper airway obstruction.
   - Short sternum is seen in trisomy 18.
   - Barrel-shaped chest is seen in emphysema, asthma and cystic fibrosis.
   - Bell-shaped chest is seen in Ellis–van Creveld syndrome.
7. Beading of costochondral junction is seen in rickets, scurvy and chondrodysplasia. Their differentiating features are given in Table 3.20.
8. Palpable costochondral junction is seen in severely malnourished child with marasmus.
9. Harrison's sulcus is a groove seen along the insertion of the diaphragm. This condition

TABLE 3.20 Differences between Rachitic and Scorbutic Rosary and Chondrodysplasia

Features	Rickets	Scurvy	Chondrodysplasia
Pathology	Epiphyseal widening	Subluxation of the joint due to defective collagen	Dysplasia of bones
Beading	Rounded	Angulated	Rounded
Tenderness	Non-tender	Tender	Non-tender
Sternum	Prominent	Pushed backwards	Prominent

occurs due to constant pulling of the soft ribs by the diaphragm. It is seen in rickets (Fig. 3.10).

10. Bony tenderness (sternal) is seen in leukaemias.

Gynaecomastia

Enlargement of breasts in males is known as gynaecomastia. It is common during puberty. Causes of gynaecomastia are as follows:

1. Imbalance of testosterone and oestrogen levels
   - Decrease in androgen levels—it maybe due to end organ resistance to androgen, decreased synthesis of testosterone and 5-alpha reductase deficiency. Causes are testicular atrophy, absent testis and old age
   - Oestrogen excess—infancy and puberty
2. Drugs
   - Drugs affecting cardiovascular system—digitalis and spironolactone
   - Oestrogen-containing drugs
   - Antiulcer drugs—ranitidine, cimetidine and lansoprazole
   - Antidepressants
   - Recreational drugs—cannabis, anabolic steroids, alcohol and heroin
3. Tumours
   - HCG-secreting tumours
   - Oestrogen-secreting tumours of testes and adrenal glands
4. Genetic causes
   - Klinefelter's syndrome
   - Kallman's syndrome
5. Chronic diseases
   - Chronic kidney disease
   - Chronic liver disease
6. Miscellaneous
   - Acromegaly
   - Thyrotoxicosis

Examination from Back

Always examine the child from behind (with the patient sitting). Inspect and palpate the respiratory movements of the chest from behind. The movements are decreased in collapse, fibrosis of lung, foreign body obstruction and pleural fluid. Note deformities of the spine—kyphosis and scoliosis in the thoracic area.

GENITALIA

Male Genitalia

In males, both the testes and the penis should be examined. The clinician should also look for the presence of any unusual findings such as absence of pubic hair, abnormal genitalia, swellings, atrophy or absence of testes and small penis. Always look for the presence of testes at an abnormal site if it is absent in the scrotum.

Penis

The examiner should look for any abnormal findings such as phimosis, hypospadias and micropenis. If the child has ambiguous genitalia, it would be difficult to ascertain the sex of the child by examining the genitals.

The penile length should be noted. The normal penile lengths at various ages are given below.

Age	Penile length (cm)
Birth	4
4 years	5
11 years	6
Adolescent	12

Micropenis—if the length of the stretched penis is <1.5 cm, it is called micropenis. Causes of micropenis are as follows:

- Carpenter's syndrome
- Cornelia de Lange syndrome

- Down's syndrome
- Hypopituitarism
- Klinefelter's syndrome
- Prader–Willi syndrome
- X-linked hypogammaglobulinaemia

Testis

The examiner should palpate the testis on both sides and assess the testicular volume. Absence of testis or undescended testis should also be noted.

Testicular Volume. The volume of testes depends upon the age of the child and his sexual growth. Sexual growth is measured by sexual maturity rating (SMR). The testicular volume is measured by the following methods:

- Ordinary ruler
- Orchidometer (Fig. 3.22)
- Ultrasonogram

The measurement of testicular volume is done most commonly by rulers due to the simplicity and cost effectiveness of this method. The normal testicular volumes are given below.

Stage	Testicular volume (cm^3)
Before puberty	1
At stage II puberty	2–3.2
At stage III puberty	3–3.4
At stage IV puberty	4.1–4.9
At stage V puberty	5

A decreased testicular volume indicates testicular atrophy and should be evaluated further for hormone deficiency. An increased testicular volume should arouse a suspicion of tumours of testis.

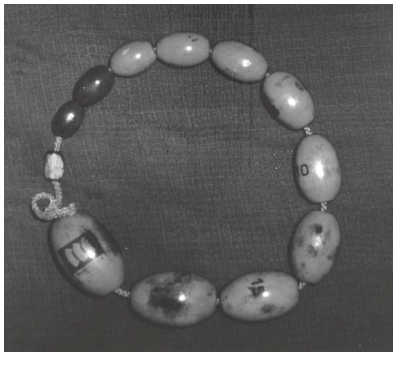


FIGURE 3.22 Orchidometer—to measure testicular volume.

Spermatic Cord

Spermatic cord is palpated from behind the neck of the scrotum. It contains vas deferens, which feels like a thick string inside the spermatic cord.

Female Genitalia

The examination of female genitalia should always be done in the presence of a female attendant. The purpose and the method of examination should be explained to the parents and the child. The consent should be obtained from the parents if the child is small. The consent should be obtained both from the parents and the child if the child is old enough to understand.

Look for discharge or bleeding. In a newborn, there may be vaginal bleeding due to withdrawal of maternal hormones. In the presence of infection, abnormal discharge may be seen. Gynaecological examination is done when indicated in adolescents.

Ambiguous Genitalia

Careful examination should be done so that ambiguous genitalia are not missed. Look for normal appearance of the male or female genitalia. The sex of the child should be ascertained by examining the genitalia. In female children with ambiguous genitalia, the testes may be palpated.

RECTAL EXAMINATION

Rectal examination is done when indicated. It is important in children with anorectal anomalies. It helps to differentiate between congenital and acquired megacolon. In congenital megacolon the rectum is empty, and in acquired megacolon the rectum is loaded with stools.

Examining Finger Specifications

For rectal examination in newborns and infants, the examiner should use the little finger. In older children, the index finger can be used for rectal examination.

Position of the Patient

The child should be asked to lie in the left lateral position, with the thighs flexed over the hips and the knees drawn up.

Procedure

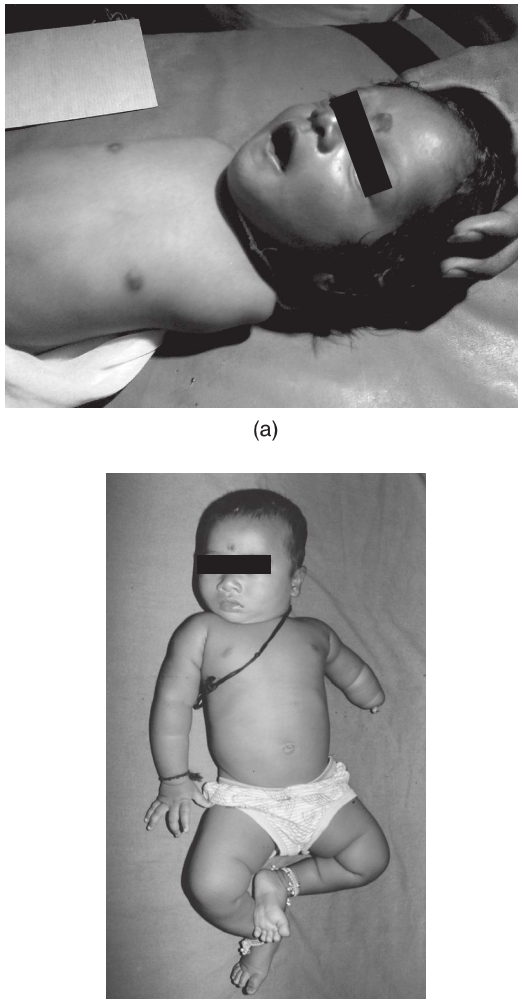
The examiner should lubricate the gloved hand and stand behind the patient facing the patient's feet. The pulp of the finger should be placed flat on the anus so that the volar aspect of the finger touches the anus. The examiner should then, without flexing the finger, press firmly at its tip to make the finger enter the rectum. If there is any pain, the rectal examination should be stopped.

With the finger inside the anus, the examiner should feel for any abnormalities in the rectal cavity or in the walls of the rectum. The finger should be rotated through 360° to examine all parts of the rectum. Then the finger should be brought to the anorectal area to feel for the contraction of the external sphincter muscle. This can be felt as a reflex contraction or by asking the patient to contract the sphincter voluntarily. Parts to be felt during rectal examination are given below.

Direction of rectal examination	Parts to be palpated
Anteriorly	Rectovesical pouch, seminal vesicles and prostate can be palpated in males In females, the cervix is palpated
Laterally	The side walls of the rectum are palpated. It is possible to reach up to the side walls of the pelvis
Posteriorly	The hollow of the sacrum and the coccyx are felt

EXTREMITIES

Ectromelia is a condition in which an individual extremity is absent or underdeveloped. For example, amelia (Fig. 3.23) is the congenital absence of one or more extremities and hemimelia is a defect in the distal part of the extremities. Phocomelia is a condition where the forearms and arms in the upper limbs or thighs and legs in the lower limbs may be absent, and the hands and feet may arise directly from the trunk. This is the complete form. In incomplete form, the deficiency is only proximal or distal, that is either arms and thighs are missing or only forearms or legs are missing.



(a)

(b)

FIGURE 3.23 (a) Amelia—absence of a limb. (b) Phocomelia—absence of partial limb.

Upper Limbs

Examination of upper limbs is important, as it gives valuable information about other systems as well. For instance, the radial pulse examination is

a part of cardiovascular examination. The reflexes elicited in the upper limbs give information about the neurological status of the patient. Nutritional status can be assessed by the midarm circumference and the skin changes in malnutrition. Also, study of the dermatological pattern in the palms and soles (dermatoglyphics) gives information about the type of chromosomal disorders. For example, simian crease is a feature of Down's syndrome. Hence, a careful examination should be done. Examination of the upper limbs includes the following:

- General examination of arms and hands—look for deformities such as claw hand, amelia, hemimelia, presence of extra digits, etc.
- Examination of axilla including axillary lymph nodes
- State of arterial wall of radial and brachial arteries
- Examination of muscles for muscle wasting, power, tone and any fasciculation
- Cubitus valgus—increased carrying angle at the elbow is seen in Turner's syndrome
- Wrist widening—rickets
- Involuntary movements—liver flap (wing beating tremor) in liver failure
- Palmar erythema—in liver failure
- Dupuytren's contracture—in liver failure
- Tests for reflexes—biceps, triceps and supinator reflexes. Also examine for Hoffmann's sign and Wartenberg's sign (see Chapter 11)
- Tests for coordination—finger–finger test, finger–nose test and dysdiadochokinesia
- Cutaneous sensations—check all modalities to exclude root or nerve lesions
- Examination of joints for movements, tenderness and inflammation, if any

Trident Hand

The hands are short and stubby, with gap between the middle and ring fingers to give it a fork-like appearance. It is seen in chondrodystrophy.

Trident sign is the divergence between the third and the fourth digits in hand in achondroplasia.

Absent Radius

- Thrombocytopenia with absent radius (TAR) syndrome
- Holt–Oram syndrome is associated with aplasia or hypoplasia of thumb and radius
- Fanconi's pancytopenia may be associated with absent thumb and radius

Fingers

The fingers should be examined carefully for disorders that manifest with changes in them. The fingers should be examined for any abnormality in their number and length. Any abnormal fusion of fingers should be noted. The pattern of ridges and arches may give clue to the type of chromosomal disorder present in the child.

Clubbing

Clubbing is a bulbous enlargement of the distal portion of terminal phalanx due to proliferation of subungual connective tissue. Clubbed fingers are frequently called serpent's hand or 'Hippocratic fingers', as they were first described by Hippocrates. Clubbing is characterised by the following symptoms:

- Subcutaneous swelling involving the root of nail. This condition results in the fluctuation and softening of nail bed.
- Obliteration of the *Lovibond angle*, that is, the angle between the nail bed and the proximal nail fold (cuticle). The normal angle is 160° (Fig. 3.24).

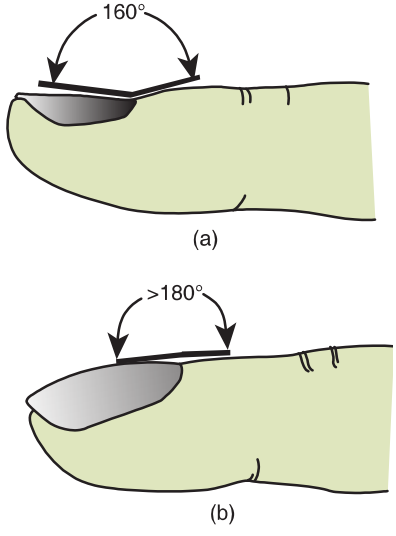


FIGURE 3.24 Lovibond angle. (a) Normal. (b) Obliterated.

- *Schamroth's sign or Schamroth's window test*—When the dorsal side of the corresponding digits of opposite hands are placed opposite to each other so that the nails are in contact, a quadrangular (diamond-shaped) space is seen in normal subjects. This is obliterated in the presence of clubbing. This is called positive Schamroth's sign (Fig. 3.25a).
- Increased convexity of the nail in both the vertical and the transverse directions.
- Thickening of the whole distal finger. This is measured by the *phalangeal depth ratio*. It is the ratio of distal phalangeal depth (DPD) to interphalangeal joint depth (IPD) and is usually measured in index finger. This ratio is greater than 1 in presence of clubbing. Normally, DPD is less than IPD (Fig. 3.25b).
- Loss of longitudinal ridges of the nail.

How to Elicit? The clubbing usually affects the thumb and forefinger first. Hold the forefinger with both the thumbs. Place both the index fingers on either side near the base of the nail. Apply pressure with one index finger and feel the movement by the other finger. In early stage of clubbing, there will be fluctuation at the base of the nail due to soft tissue proliferation. In normal children, there will be no fluctuation.

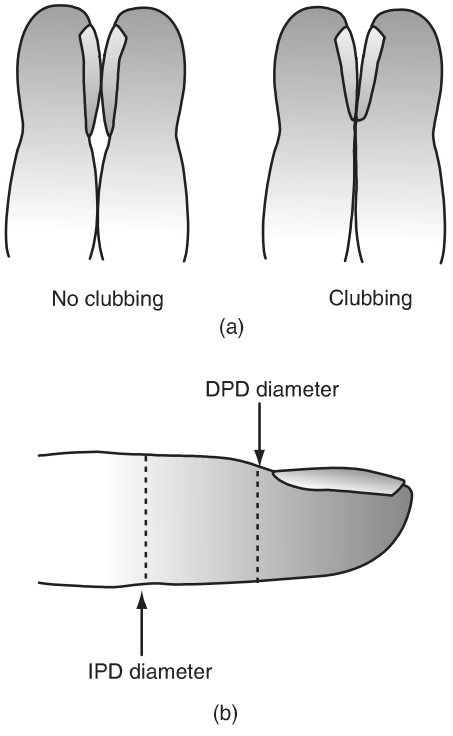


FIGURE 3.25 (a) Schamroth's sign. (b) DPD and IPD. DPD: IPD ratio is less than 1 in normal children and more than 1 in clubbing.

Aetiopathogenesis

- Cyanotic heart disease is associated with hypoxia. This results in the formation of arteriovenous fistula, which results in shunting of blood.
- Reduced ferritin is increased, resulting in vasodilatation and formation of arteriovenous anastomosis. Usually, the ferritin is oxidised in the lungs. However, in conditions where the blood bypasses the lungs, the ferritin will escape degradation and enter systemic circulation and cause vasodilatation.
- Other substances that cause vasodilatation and formation of arteriovenous anastomosis are adenosine triphosphate, 5-hydroxy tryptamine and prostaglandins (PGE2).
- Hormonal theory—Tumours or the diseased lung tissue elaborate the hormones that may cause vasodilation in the distal limbs. Increased oestrogen levels cause vasodilatation. Increased levels of growth hormone and parathormone result in clubbing.
- Tumour necrosis factor (TNF), platelet-derived growth factor (PDGF) and hepatocyte growth factor cause connective tissue proliferation.
- Neurogenic theory—Afferent impulses from lungs to the brainstem through intercostal and vagus nerves cause reflex vasodilatation. Resection of these nerves will relieve clubbing.
- Genetic predisposition—Autosomal-dominant gene is one of the causes for clubbing.

Grading. Grading of clubbing can give some clues about the cause of clubbing. Lesser grade of clubbing (parrot beak type) is seen in fibrocaseous pulmonary tuberculosis, inflammatory bowel diseases and polyposis of colon. The grade of clubbing is higher (drumstick type) in cyanotic congenital heart diseases and chronic suppurative lung diseases such as empyema and bronchiectasis (Fig. 3.26).

Hypertrophic pulmonary osteoarthropathy is associated with clubbing and thickening of the periosteum of radius, ulna, tibia and fibula. This

condition is seen in bronchiectasis, cirrhosis of liver, mesothelioma, etc.

Grade	Features
I	Fluctuation and softening of nail bed
II	Obliteration of the nail bed angle (Schamroth's sign). Normal Lovibond angle is <165°
III	Parrot beak appearance (increased convexity of nail fold) Drumstick appearance due to thickening of the whole distal finger
IV	Swelling of fingers in all dimensions, associated with hypertrophic pulmonary osteoarthropathy (pain and swelling of wrists and hands, with radiographic evidence of new subperiosteal bone formation)

Pierre–Marie–Bamberger disease is a special form of hypertrophic pulmonary osteoarthropathy. This disease is a combination of clubbing and thickening of periosteum and synovium. It is commonly seen in patients with lung cancer.

Pulmonary hypertrophic osteoarthropathy is a hereditary condition in which clubbing is seen without any underlying pathology.

Acute and Chronic Clubbing. Clubbing may be acute or may develop over a long period. For instance, in cyanotic heart disease, it may take about 6 months, and, in bronchiectasis, it may take up to 1 year for clubbing to develop.

Acute clubbing (develops within 2–3 weeks)

- Suppurative lung disorders (in lung abscess, clubbing may be seen in 10–14 days)
- Infective endocarditis
- Mesothelioma

Chronic clubbing develops in about 6 months in cyanotic heart diseases such as tetralogy of Fallot (TOF). In bronchiectasis, it may take about 1 year for the clubbing to develop.

Causes

- A-V malformations
- Major vessel abnormality—aneurysm of brachial artery, aneurysm of subclavian or innominate artery
- Thoracic outlet syndrome—causing obstruction of blood flow to the limbs as in cervical rib
- Pancoast tumour—refers to the lung malignancy occurring at the apex. It is rare in children

Causes of *unidigital clubbing* are as follows:

- Trauma
- Gout
- Sarcoidosis

Bilateral clubbing may be congenital or acquired. Acquired causes of bilateral clubbing include the following:

1. Primary
   (a) Idiopathic



(a)



(b)

FIGURE 3.26 Grade III clubbing. (a) Parrot beak appearance (also note the obliterated lovibond angle). (b) Drum stick appearance.

(b) Familial—it is seen in certain families without any known cause in the second or third decade of life. It is inherited as an autosomal-dominant pattern. These children do not require any intervention

2. Secondary
   (a) Cardiovascular
      - Cyanotic heart disease
      - Subacute bacterial endocarditis
      - Chronic congestive cardiac failure (CCF)
   (b) Respiratory
      - Suppurative—bronchiectasis, lung abscess, empyema and pulmonary tuberculosis
      - Neoplastic—bronchial adenoma, mesothelioma and bronchogenic carcinoma (common in adults)
   (c) Abdominal
      - Cirrhosis
      - Malabsorption syndrome
      - Intestinal polyposis
      - Inflammatory bowel disease—ulcerative colitis, Crohn's disease
   (d) Endocrine
      - Myxoedema
      - Thyrotoxicosis

Clubbing with Other Associated Signs. Clubbing may also be associated with cyanosis (Table 3.21) or tenderness. Association of clubbing with tenderness is seen in the following conditions:

TABLE 3.21 Association of Clubbing with Cyanosis

Association	Conditions
Clubbing without cyanosis	Subacute bacterial endocarditis Ulcerative colitis Healthy individual (familial cases) Cirrhosis
Cyanosis without clubbing	All types of peripheral cyanosis Abrupt onset of central cyanosis Mitral stenosis
Cyanosis with clubbing	Cyanotic heart disease Pulmonary arteriovenous shunts Lung abscess (rare)

- Infective endocarditis
- Suppurative lung disorders
- Mesothelioma

Differential Clubbing. It refers to the clubbing with cyanosis that is limited to the upper or lower limbs.

- Clubbing with cyanosis limited to lower limbs is seen in patients with patent ductus arteriosus (PDA) with a reversed shunt.
- Clubbing with cyanosis limited to the upper limbs is seen in children with transposition of great vessels (TGA) with PDA with a reversed shunt.

Pseudoclubbing. As the name suggests, it refers to the appearance of clubbing without it being actually present. It is seen in the following cases:

- Hyperparathyroidism—there is excessive resorption of the distal phalanx
- Hansen's disease—damage to the fingers due to sensory neuropathy
- Leukaemia with secondary deposits in the bone results in destruction of bones

Polydactyly

It is a condition where there are more than five digits in the limbs (Fig. 3.27). Polydactyly can be congenital or familial. It is commonly associated with the following syndromes:

- Laurence–Moon–Biedl syndrome
- Turner's syndrome
- Carpenter's syndrome



FIGURE 3.27 Polydactyly.

- Ellis–van Creveld syndrome
- Trisomy 13
- Orofaciodigital syndrome
- Rubinstein–Taybi syndrome
- Meckel–Gruber syndrome

Syndactyly is a condition where there is a fusion or webbing of two or more digits. It is commonly associated with the following syndromes:

- Apert's syndrome
- Carpenter's syndrome
- De Lange syndrome
- Holt–Oram syndrome
- Trisomy 21, 13 and 18 chromosomes
- Foetal hydantoin syndrome
- Laurence–Moon–Biedl syndrome
- Fanconi's syndrome

Arachnodactyly

It is a condition where the fingers and toes are abnormally long and thin. Arachnodactyly is commonly associated with the following conditions:

- Marfan's syndrome
- Hypogonadism
- Homocystinuria
- Hypopituitarism
- Normal variant

Macrodactyly

It is an enlargement of a digit and is usually idiopathic. It is also seen in the following conditions:

- Neurofibromatosis
- Ollier's disease
- Maffucci's syndrome
- Congenital lymphoedema

Aplasia of Digits (Absence of Digits)

It is a condition in which one or more digits are absent due to defective development. It may be congenital and associated with the following conditions:

- Fanconi's anaemia—congenital aplastic anaemia associated with absent thumb
- Holt–Oram syndrome—absent thumb

Thumb Sign

Clench the wrist with the thumb held in the palms. Tip of the thumb will protrude past the ulnar border of the hand in Marfan's syndrome.

Clinodactyly

It refers to a curved little finger (Fig. 3.28). Congenital radial or ulnar deviation of the little finger occurs due to hypoplasia of middle phalanx. Clinodactyly can be seen in the following conditions:

- Normal variant
- Aarskog syndrome
- Cornelia de Lange syndrome
- Trisomy 21 (Down's syndrome)

Camptodactyly

It refers to congenital anteroposterior flexion deformity at the metacarpophalangeal joint and proximal interphalangeal joint of the fingers (Fig. 3.29). It is unrelated to trauma, systemic disease or neurological abnormality. It is usually seen in the little finger. Characteristic features are the following:

- Minimal flexion contracture
- Firm tender swelling in proximal interphalangeal joint
- Fibrotic changes



FIGURE 3.28 Clinodactyly.

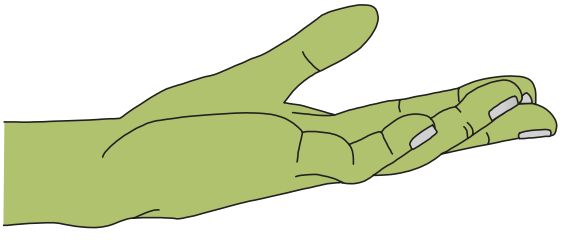


FIGURE 3.29 Camptodactyly.

Camptodactyly is associated with the following conditions:

- Familial arthritis
- Marfan's syndrome
- Weaver–Smith syndrome

Low Set Thumbs

Low set thumbs are seen in patients with Down's syndrome.

The set of the thumb is the vertical distance from the thumb's insertion point down to the wrist. In high set thumbs, this distance is greater so that the thumbs are far from wrist and close to the fingers. In low set thumbs, the thumb is closer to the wrist.

Dermatoglyphics

It is the scientific study of finger prints. It refers to the study of the skin ridge patterns on fingers, toes, palms and soles. Uses are as follows:

- Identification: The pattern is specific for each individual. No two people can have the same pattern.
- Diagnosis of chromosomal disorders: The pattern of changes is typical for certain chromosomal disorders and thus helps identify the type of chromosomal abnormalities such as Down's syndrome and Turner's syndrome. Table 3.22 summarises the dermatoglyphics seen in various disorders.

Skin ridges are formed during the critical period of embryogenesis, that is, between 4 weeks and 5 months of gestational age. This is the period during which the major organs develop.

A *triradius* is a point where the pattern deviates into three directions (Fig. 3.30). There are three types of patterns:

Patterns	Number of triradius
Simple arch	No triradius
Loop	One triradius
Whorl	Two triradii

The proximal triradius in the palm close to the wrist is designated as 't'. The four other triradii

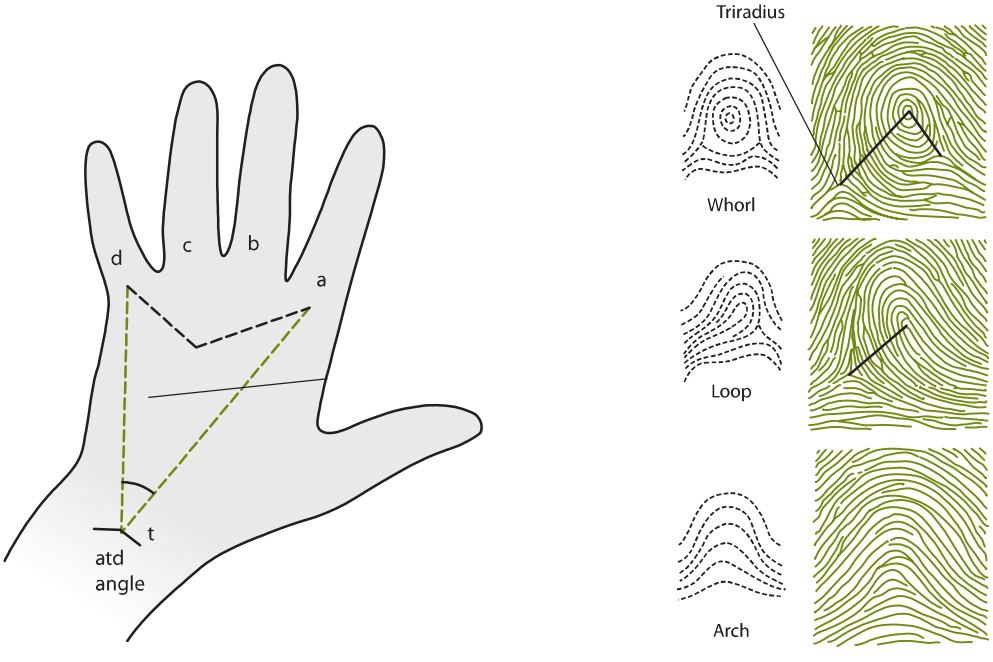


FIGURE 3.30 Dermatoglyphics. (a) atd angle. (b) Skin ridge patterns.

TABLE 3.22 Dermatoglyphics in Various Disorders

Syndromes/ Disorders	Dermatoglyphics
Down's syndrome	Mainly ulnar loops on most fingers. Radial loops on fingers 4 and 5 Increased 'atd' angle (distal axial triradius) Simian crease Sydney line Kennedy crease Single crease on the fifth digit Low a–b ridge count. Increased incidence of skin ridge dissociations. Lower ridge counts along the digital midlines, especially in the little finger Transverse alignment of skin ridges in interdigital area Soles—tibial arch (arch pattern seen on the tibial side of the soles) or small loop distal in the hallucal area
Turner's syndrome	Predominance of whorls Low ridge count
Klinefelter's syndrome	Excess of arches on the first digit Excess of ulnar loops on the second digit
Trisomy 18 (Edward's syndrome)	6–10 arches Single transverse palmar crease Single crease on the fifth digit or all digits
Trisomy 13 (Patau's syndrome)	Excess of arches on finger tips and soles Simian crease Increased 'atd' angle (distal axial triradius) Soles—fibular arch in the hallucial (great toe) area
Noonan's syndrome	Increased frequency of whorls on fingertips Axial triradius 't' as in Turner's syndrome Single transverse palmar crease

situated on the index, middle, ring and little fingers are designated as 'a', 'b', 'c' and 'd', respectively. The angle between the triradii 'a', 't' and 'd' is known as the 'atd' angle. It is usually 40°. The 'atd' angle changes as the person ages. It is obtuse in Down's syndrome and Turner's syndrome as the proximal triradius 't' is shifted distally.

Fingerprint Pattern

The examiner should look for the pattern of arches, loops and whorls on the fingertips. Some conditions are associated with the same pattern in all the fingers. Such abnormal patterns of fingerprints are as follows:

Pattern	Condition
Ulnar loops on most of the fingers (ridges slope towards the little finger)	Down's syndrome
Arch	Trisomy 18
Whorl	Congenital rubella syndrome

Palmar Crease Pattern

Simian Crease. It refers to a single palmar crease. It is formed by the fusion of two distal creases and is associated with Down's syndrome (Fig. 3.31).

Sydney Line. Two transverse creases are normally seen in the palm. If the proximal one runs across the entire palm, it is called a Sydney line. This line is seen in patients with Down's syndrome and congenital rubella syndrome.

Number of Ridges. Count the total number of ridges from the core of the pattern to the triradius. The total from all the 10 fingers will be as follows:

- Males—145
- Females—127

Plantar Crease Pattern

The normal plantar crease pattern should be examined by taking the foot prints.



FIGURE 3.31 Simian crease.

Kennedy Crease. It refers to a deep sole crease between the first and the second toes. It is seen in Down's syndrome.

Lower Limbs

The lower limbs should be examined after exposing them from groin to the toes. The legs should be examined with the child in supine, prone and standing positions. The child should also be observed while walking so that abnormalities of gait become evident.

The lower limb length is measured from anterior superior iliac spine to the lower end of the medial malleolus on both sides.

The atrophy or wasting of the limbs can be assessed by measuring the circumference at the same level above or below the patella.

During the examination of lower limbs, the clinician should pay attention to the following:

1. General examination of legs and feet
   - Limb length—decreased in rickets
   - Intercondylar distance and intermalleolar distance—increased in rickets
   - Double malleoli—rickets
   - Genu valgum or varus—rickets (Table 3.23)
   - Coxa vara—rickets
2. Tests for power, tone, reflexes (including plantar response) and coordination
3. Examination of joints for movements, pain, swelling or deformities, such as genu varum and genu valgum (Fig. 3.32). Genu recurvatum is hyperextensibility of the knee joint (Fig. 3.33). This is seen in conditions where the ligaments appear lax
4. Examination of muscles for wasting or fasciculation
5. Peripheral pulses—femoral, posterior tibial and dorsalis pedis arteries
6. Temperature of feet—decreased in shock
7. Pedal oedema—hypoproteinaemia due to liver failure, renal disease and CCF
8. Stance, balance and gait
   - Ataxic gait—Wilson's disease
   - Waddling gait—rickets

TABLE 3.23 Genu Varum and Valgum

Deformity	Description	Associated Conditions
Genu varum (bow legs)	The knees are bowed outside and the inter-condylar distance is increased (more than 10 cm)	Rickets Osteomalacia Achondroplasia Osteitis deformans (rare in children) Normal variant in children below 2 years of age
Genu valgum (knock knees)	The knees are close to each other and the intermalleolar distance is increased	Congenital condition, a normal variant Rickets

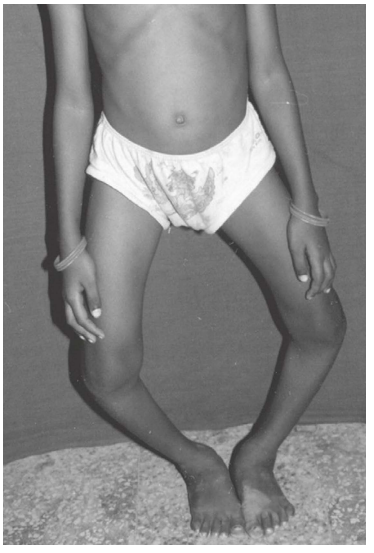


FIGURE 3.32 Genu varum (bow legs).



FIGURE 3.33 Genu recurvatum.

Feet

The feet should be examined for normal shape and movements, both at rest and while walking. Some abnormalities that are not evident at rest may become evident while walking. Also observe the part that is in contact with the floor while standing. Some abnormal findings in examination of feet include the following:

1. Rocker bottom foot (congenital vertical talus) with prominent calcaneum and rounded bottom is seen in Edward's syndrome (trisomy 18) and Patau's syndrome
2. Pes planus (flat foot) is a condition where the longitudinal arch is absent. As a result, there is an increased area of ground contact of the foot with weight bearing on the legs. This condition is associated with the eversion of fore foot and hallux valgus. Physiological flat foot is flexible. It is seen in infants, toddlers and 15% of the adults. Pathological flat foot is stiff and has a tight heel cord. Flat foot may be seen in the following conditions:
   - Familial inheritance
   - Cerebral palsy
   - Defects of the spinal cord—myelodysplasia
   - Ehlers–Danlos syndrome
   - Marfan's syndrome
   - Osteogenesis imperfecta
   - Muscular dystrophy
3. Pes cavus (claw foot) is a condition where the longitudinal arch is high. It is associated with the following conditions:
   - Anterior poliomyelitis
   - Bony defects—metatarsus varus (adduction and inversion of foot)
   - Cord lesions—syringomyelia, spina bifida and diastematomyelia equine (cauda equina) lesions
   - Genetic—Refsum's disease, Friedreich's ataxia and Hurler's syndrome
   - Idiopathic
   - Peroneal muscular atrophy
4. Clawed toes occur due to flexion contracture of proximal and distal interphalangeal joints. These are seen in the following conditions:
   - Friedrich's ataxia
   - Peroneal muscular atrophy
5. Varus toes—one toe lies above or below the adjoining medial toe
6. Hammer toe refers to the condition where the toe is held in flexion due to flexion contracture of proximal interphalangeal joint. It may be congenital (e.g., trisomy 18) or acquired (e.g., pes cavus)
7. Club foot (congenital talipes equinovarus) (Fig. 3.34)—the components in the foot are as follows:
   - Adduction of fore foot
   - Inversion of hind foot
   - Medial rotation
   - Varus deformity
   - Equinus deformity (plantar flexion). Dorsiflexion is not possible
8. Camptodactyly
9. Pitting oedema in the ankles and the dorsal surface of the feet is seen in CCF. This is also known as dependent oedema

In a case with suspected shock or vascular insufficiency, the clinician should look for the following:

1. Peripheral pulse at the dorsalis pedis and posterior tibial artery: These pulses are either feeble or absent in shock and coarctation of aorta. In arterial obstruction, the pulses are absent.
2. Capillary refill time: The sole is pressed to cause blanching. The time taken for filling of



FIGURE 3.34 Bilateral club feet.

the blanched area on release of the pressure is noted. The normal time is less than 3 seconds. In patients with shock or vascular insufficiency, the refilling time is more than 3 seconds.

3. Temperature of the feet: The feet are cold in shock.

OEDEMA

Oedema is a swelling of the tissue due to accumulation of fluid. It may be pitting or non-pitting. To identify the type of oedema, press on the skin over a bony area for 10 seconds. If there is no pitting, it is called *non-pitting oedema*. Non-pitting oedema occurs due to lymphatic obstruction. If the pitting persists after removal of the pressure, it is called *pitting oedema*. If the pitting remains for more than 1 minute, it is called a *slow oedema*, which occurs due to congestion. If the pitting disappears within 40 seconds, it is known as *fast oedema*, which arises due to hypoalbuminaemia.

SKIN

Thorough history and physical examination are necessary to diagnose a skin lesion and avoid missing any finding of importance. The lesions in the skin may be primary lesions or secondary to systemic disorders. The following abnormalities should be specifically looked for while examining the skin:

- Colour changes—pallor and jaundice
- Pigmentation—hypo- or hyperpigmentation. Diffuse hyperpigmentation is seen in Addison's disease
- Scratch marks—seen in cholestasis
- Scars
- Skin lesions due to vascular pathology—skin bleeds such as purpura, ecchymosis are seen in cirrhosis, thrombocytopenia, vitamin K deficiency in malabsorption of fat, etc.
- Skin lesions due to ingestion of drugs—Steven Johnson syndrome (sulfa drugs) (Fig. 3.35)
- Rashes—measles and chicken pox
- Skin infections—impetigo and scabies (Fig. 3.36)
- Turgor—decreased in dehydration and marasmus and increased in hypernatraemic dehydration
- Signs of PEM



FIGURE 3.35 Skin lesions due to Steven Johnson syndrome. The child has oedema and erythema of lips and buccal mucosa, erythematous macules, haemorrhagic crusting, ulcerations, vesicles, bullae and areas of denudation on the body.



FIGURE 3.36 Impetigo.

- Signs of vitamin deficiency (dermatitis)
- Erythema nodosum—tuberculous abdomen and crohn's disease
- Subcutaneous nodules
- Striae
- Xanthomas—chronic cholestasis, glycogen storage disorder Type I and hyperlipidaemias

Colour

The colour of the skin depends upon the blood flow to the skin. Various pathological conditions also present with colour changes in the skin (Table 3.24). Various skin colour changes that should be looked for include pallor, cyanosis, jaundice and pigmentary changes (Fig. 3.37).

Pallor

Pallor is the paleness of the skin. The presence of pallor depends on the thickness and quality of skin and the

TABLE 3.24 Colour Changes of the Body in Various Conditions

Colour	Conditions
Pink	Normal
Pale (pallor)	Severe anaemia and shock
Blue (cyanosis)	Cyanotic heart disease, Eisenmenger's syndrome, sulphaemoglobinaemia and methaemoglobinaemia
Yellow (icterus)	Jaundice and carotenaemia
Pale lemon yellow	Haemolytic anaemia
Greenish yellow/dark yellow	Obstructive jaundice
Orange yellow	Hepatocellular jaundice and xanthomatosis
Slaty grey	Argyria—silver poisoning
Cherry red	Carbon monoxide poisoning
Harlequin colour change	In this condition, the body is differently coloured in two vertical halves. One half of the body is pale, while the other half is deep red. This occurs due to autonomic disturbances. This pattern changes with the change in position and lasts for few minutes
Blue peripheries	Acrocyanosis
Black	Addison's disease—pigmentation in the exposed areas
Grey	Grey baby syndrome—chloramphenicol



FIGURE 3.37 Harlequin colour change.

amount and quality of the blood in the capillaries. Pallor may be due to any of the following reasons:

1. Pallor due to thick skin
   - Hypopituitarism
   - Hypothyroidism
2. Pallor due to decreased blood flow
   - Shock
   - Left heart failure
   - Vascular insufficiency due to obstruction of blood vessels or vasoconstriction
3. Pallor with normal blood flow
   - Severe anaemia

Cyanosis

Cyanosis refers to the bluish discolouration of the skin and mucous membranes. It occurs due to the presence of more than 5 g% of reduced haemoglobin in the blood. It also occurs due to the presence of abnormal haemoglobin. The sites at which cyanosis is likely to be evident are the following:

- Nail bed
- Lips
- Tongue
- Conjunctiva
- Oral cavity mucosa
- Ear lobes

Depending on the mechanism and causes, cyanosis may be central, peripheral, mixed or differential.

Central Cyanosis. It occurs due to the presence of more than 5 g% of reduced haemoglobin in the blood. Usually 30% of the total haemoglobin is reduced. Hence, in patients with severe anaemia, since haemoglobin level is low, the cyanosis may not be evident. In polycythaemia, cyanosis may be seen even if less than 30% of the total haemoglobin is reduced. The causes of central cyanosis include the following:

1. Decreased atmospheric oxygen and high altitude
2. Respiratory causes—respiratory failure or impaired pulmonary functions due to the following factors:
   - Alveolar hypoventilation—airway obstruction due to acute severe asthma

- Ventilation-perfusion mismatch (imbalance between ventilation and perfusion)—foreign body obstruction
- Impaired oxygen diffusion—interstitial pneumonia

3. Anatomic shunts
   - Cardiovascular causes—congenital heart diseases such as TOF, TGA, truncus arteriosus, total anomalous pulmonary venous drainage and Eisenmenger's complex
   - Pulmonary causes—pulmonary arteriovenous fistula and multiple intrapulmonary shunts

   Differences between cyanosis due to cardiac cause and respiratory cause are discussed in Table 3.25.
4. Abnormal haemoglobins—the abnormal haemoglobin level in normal children is approximately 1%–2% of the total haemoglobin level. Excessive levels are present when the haemoglobin is oxidised by drugs or chemicals such as phenacetin, sulphonamides, aniline dyes, nitrates and nitrites
   - Methaemoglobinaemia—methaemoglobin is an oxidised derivative of haemoglobin. Its level is more than 1.5 g% or 10% of total haemoglobin level. Differences between cardiac cyanosis and cyanosis in methaemoglobinaemia are discussed in Table 3.26
   - Sulphaemoglobinaemia—sulphaemoglobin level is more than 0.5 g%
   - Carboxyhaemoglobinaemia—it is seen in carbon monoxide poisoning. Carbon monoxide has an affinity for haemoglobin about 200 times more than that for oxygen. Less than 1% of carboxyhaemoglobin is normally present in children. A high concentration of carboxyhaemoglobin will result in tissue anoxia

TABLE 3.25 Differences between Cyanosis Due to Cardiac Cause and Respiratory Cause

Features	Cardiac Cyanosis	Respiratory Cyanosis
Symptoms	Tachypnoea	Dyspnoea
Age at onset	Early; may appear at or immediately after birth	Late
Intercostal recession with dyspnoea	Less pronounced	More pronounced
On crying	Aggravation of cyanosis	Improvement in cyanosis
Administration of oxygen (hyperoxia test)	No significant increase in partial pressure of oxygen (pO_2)	Increase in pO_2 to more than 150
Partial pressure of carbon dioxide (pCO_2)	Normal or low	May be increased

Types of central cyanosis according to pathophysiology are as follows:

- *Intermittent cyanosis:* In Ebstein's anomaly, the central cyanosis is seen intermittently.
- *Enterogenous cyanosis:* This type of central cyanosis occurs due to absorption of toxic materials from intestine, resulting in increase in methaemoglobin or sulphaemoglobin levels in the blood. The child is not dyspnoeic. Drugs causing enterogenous cyanosis are nitrates, nitrites, nitroglycerine, amyl nitrite, sodium nitroprusside, sulphonamides, dapsone, etc.
- *Orthocyanosis:* Central cyanosis is seen only in erect posture. For example, in children with pulmonary arteriovenous malformations, hypoxia occurs in erect posture.

Peripheral Cyanosis. It arises due to slowing of blood flow in an area and greater extraction of oxygen from normally saturated arterial blood in that area. The temperature of the peripheral cyanosed area is always less than the normal body temperature. Differences between central and peripheral cyanosis

TABLE 3.26 Difference between Cardiac Cyanosis and Cyanosis in Methaemoglobinaemia

Features	Cardiac Cyanosis	Cyanosis in Methaemoglobinaemia
Associated symptoms	Present	Absent
Clubbing	Present	Absent
Therapeutic trial with ascorbic acid and methylene blue	No improvement	Improvement present
Predisposing factor	Exertion	Intake of dapsone

TABLE 3.27 Differences Between Central and Peripheral Cyanosis

Features	Central Cyanosis	Peripheral Cyanosis
Mechanism	Reduced haemoglobin >5 g%	Sluggish blood flow in the affected parts
Sites	Soft palate, tongue, floor of mouth, inner side of lip, lower palpebral conjunctiva, nail bed and earlobes	Seen only in affected parts such as the tip of the fingers and toes, palms and soles, tip of the nose and ear lobules
Involved part	Warm	Cold
Effect of inhaled oxygen	Cyanosis may improve	Does not improve
Clubbing	All digits	Absent
Polycythaemia	Present due to increased production of erythropoietin as a response to hypoxia	Absent
Effect of warmth	No change	Cyanosis decreases
Effect of cold	No change	Cyanosis increases
Dyspnoea	May be present	Absent
Administration of oxygen (hyperoxia test)	Cyanosis may improve	No change

are discussed in Table 3.27. Causes of peripheral cyanosis are as follows:

- Exposure to cold temperature: Peripheral cyanosis (acrocyanosis) due to cold environment and sluggish blood flow is commonly seen in newborns.
- Peripheral vascular disease.
- Redistribution of flow from the extremities. In birth asphyxia, the blood flow to the vital organs such as brain and heart is maintained at the expense of kidney, skin, etc. This results in decreased blood flow to the skin, leading to cyanosis. This is called diving reflex.
- Arterial and venous obstruction: Any condition causing stagnation of blood flow will result in an increased amount of reduced haemoglobin. This results in cyanosis.

Mixed Cyanosis. It occurs due to decreased oxygenation and sluggish blood flow. Causes of mixed cyanosis include the following:

- Cardiogenic shock
- Acute pulmonary oedema
- CCF
- Hypotension

Differential Cyanosis. Differential cyanosis is present when the preductal (right upper extremity) oxygen saturation is higher than the postductal (lower extremity) saturation. In PDA, the deoxygenated blood directly enters the systemic circulation without entering the lungs. The part of the body distal to this shunt is therefore cyanosed. The part of the body supplied by normal oxygenated blood proximal to this shunt is normal in colour. The causes of differential cyanosis are as follows:

- PDA with reversal of shunt—cyanosis is seen in lower limbs only
- Persistent pulmonary hypertension of the newborn (PPHN)
- Left ventricular outflow obstruction
- Ductal opening proximal to the origin of left subclavian artery with reversal of shunt—cyanosis is seen in both lower limbs and left upper limb

Reverse Differential Cyanosis. It is the condition where only the upper part of the body is cyanosed and the lower part is pink. It is seen in the following conditions:

- PDA + TGV + severe pulmonary hypertension
- PDA + TGV + preductal coarctation of aorta

Differential diagnosis of cyanosis

- *Circumoral cyanosis:* Bluish discolouration around the lips (and not on the lips) may be seen in normal children and newborns. This is due to the underlying veins in this area that are visible when the normal arterial supply is diminished. It may be seen in infants during feeding and resolves spontaneously following feeding. It is also seen after the ingestion of certain drugs such as dapsone. This should not be confused with cyanosis as lips, tongue and other sites such as nail beds are pink.
- *Pseudocyanosis* is a bluish tinge of the skin and mucosae, which is usually drug induced. This condition is not caused by hypoxaemia but by the intake of drugs such as amiodarone and clomipramine.

Jaundice

Jaundice refers to the yellowish discolouration of skin, mucous membrane and conjunctiva due to excess accumulation of bile pigments in the blood. It is clinically evident when the serum bilirubin level is greater than 2 mg/dL. Normal bilirubin level is 0.3–1 mg/dL. In newborn, normal bilirubin level can be up to 15 mg/dL. This is because of physiological polycythaemia, reduced lifespan of RBCs, immaturity of liver and increased turnover of bilirubin in the newborn babies. The sites at which jaundice can be assessed are as follows:

- Skin
- Sclera
- Nail bed
- Soft palate
- Palms and soles
- Undersurface of tongue

The sclera contains more elastic tissue and has more affinity for bilirubin. It is white in colour; therefore, any change in colour is easily evident. By applying pressure over the nails, the nail bed gets blanched. Hence, it forms a white background where colour change is easily evident. Yellowish discolouration can also be seen in body fluids like CSF and synovial fluid. Such discolouration is not evident in body secretions such as saliva and tears.

The intensity of yellowish discolouration varies according to the causative factors, such as in the following instances:

- Pale or lemon yellow discolouration is seen in haemolytic jaundice where unconjugated bilirubin levels are increased.
- Dark yellow discolouration is seen in obstructive jaundice where conjugated bilirubin levels are increased. It is also associated with scratch marks. Greenish yellow discolouration may be seen when bilirubin is converted into biliverdin, which is green in colour.
- Orange–yellow tinge is seen in hepatocellular jaundice.

Differential diagnosis of jaundice includes the following:

- Yellow tint may be seen in carotenaemia due to increased intake of carotene.
- Yellowish–orange tinge is seen in xanthomatosis.

Pigmentation

Normal pigmentation of the skin depends upon the amount of melanin present in the skin. It varies according to person, place and race. Causes of abnormal pigmentation include the following:

- Brown or blue-black pigmentation of the buccal mucosa and the exposed parts of the skin in Addison's disease
- Greyish-bronze colour of the skin due to excessive melanin pigmentation in haemochromatosis
- Slaty-grey skin due to deposition of silver in argyria
- Localised symmetrical erythema or brown pigmentation over the exposed areas in pellagra
- Albinism—generalised hypopigmentation due to congenital absence of melanin (Fig. 3.38)
- Vitiligo—depigmented patches on skin without any known cause. It is common in people with autoimmune endocrine disorders

Skin Turgor

In normal condition, if the skin is pinched, it comes to the normal position as soon as it is released. However, in conditions such as severe dehydration and marasmus, the elasticity is lost and the skin remains in the same position or returns to normal position slowly after it is released.

Subcutaneous Emphysema

Subcutaneous emphysema arises due to the collection of air in the subcutaneous spaces. A crackling sensation can be felt on compressing the affected part.



FIGURE 3.38 Albinism.

Skin Lesions

The examination of skin lesions gives clue to the type of infections or disorder.

Morphology

The morphology is confirmed by both visual and tactile examination. Caution should be taken while examining skin lesions that are contagious. Disposable gloves should be worn before palpating lesions such as those of herpes simplex and herpes zoster. According to the morphological appearance, skin lesions may be of primary or secondary types (Table 3.28).

Primary Skin Lesion. A lesion that is caused directly by the disease process is called a primary skin lesion (Fig. 3.39).

Secondary Skin Lesion. A lesion that originates from a primary lesion, or occurs secondary to external factors such as scratching, trauma, infection or healing process, is called a secondary lesion.

Hess Test (Rumpel–Leede Capillary Fragility Test or Tourniquet Test)

Hess test is used to assess the capillary fragility. The sphygmomanometer cuff is tied on the arm and the pressure is elevated to a point in between the systolic and diastolic blood pressure for 5 minutes. The appearance of purpura on the forearm should be noted. The test is said to be positive if more than 20 petechiae appear in a 2.5 cm^2 area. A positive Hess test is adopted by the WHO for the diagnosis and management of dengue infections. Hess test is positive in the following cases:

- Poor platelet function
- Thrombocytopenia
- Thrombasthenia
- Scurvy



FIGURE 3.39 Purpura.

Conditions Associated with Skin Lesions

1. *Scurvy* is seen in patients with vitamin C deficiency. It presents with asymptomatic perifollicular purpuric spots in the legs.
2. *Acrodermatitis enteropathica* occurs due to zinc deficiency. There is vesiculation and ulceration around the nose, mouth, anal opening and genitalia. Acral areas such as hands and feet are involved.
3. *Drug eruptions*—drugs may sensitise the skin to sunlight.
   - Morbilliform (measles-like) rash is seen in patients with infectious mononucleosis who are taking ampicillin.
   - Acne-like rashes are seen after high-dose prednisolone therapy.
   - Erythema nodosum and erythema multiforme are caused by sulphonamides.
   - Eczema-like lesions are seen with methyldopa and phenylbutazone.
   - Generalised exfoliative dermatitis is caused by sulphonylureas and indomethacin.
4. *Erythema nodosum* results in painful, tender, red nodules commonly over the shins. The lesions fade slowly over weeks, leaving bruises. Causes of erythema nodosum are as follows:
   - Tuberculosis
   - Behcet's disease
   - Lymphogranuloma venerum
   - Leprosy
   - Inflammatory bowel disease
   - Sarcoidosis
   - Sulphonamides
   - Streptococcal infections
   - Systemic mycosis
   - Toxoplasmosis
5. *Xanthoma* is yellow or orange papules in the

TABLE 3.28 Skin Lesions

Lesions	Description of Lesions
Primary skin lesions	
Erythema	It is redness of the skin. It is seen in inflammation or infections of skin such as streptococcal infection.
Macule	In this lesion, the colour of the skin is changed without any elevation as compared to the surrounding skin. It is seen in early stages of measles.
Papule	In this lesion, there is an elevation of the skin in the involved area. The size of a papule is usually <0.5 cm in diameter. It is seen in later stages of measles.
Nodule	Palpable lesion of >0.5 cm in diameter. It is seen in erythema nodosum.
Plaques	Circumscribed flat areas of abnormal skin, which are raised or sunk below the level of the surrounding skin. The lesion is more than 2 cm in size. This is commonly seen in conditions such as psoriasis and morphoea (localised scleroderma). Plaques may also represent thickening of the skin by infiltration of inflammatory or neoplastic cells.
Papilloma	Pedunculated lesions in the area where the mass is attached to the skin by a narrow pedicle. It is seen in viral warts.
Vesicle	Small fluid-containing lesion that is raised from the surface of the skin. It is seen in chicken pox. Vesicles are <0.5 cm in diameter.
Bullae or blisters	Large vesicles >0.5 cm in diameter. They may be uni- or multilocular and intra- or subepidermal. Bullae may contain serum, seropurulent or haemorrhagic fluid.
Pustule	Vesicles or blisters containing pus.
Wheals	Elevations of the skin caused by acute oedema of the dermis. They are flat topped and are of variable size. They are caused by the temporary increased permeability of the dermal capillaries due to local histamine release from the mast cells. Often there is a surrounding erythematous macular flare. They are seen in urticaria (hives and nettle rash).
Burrows	Burrows are short, linear, straight or sinuous elevations of the outer epidermis, usually dark in colour. They are characteristic of infestation by scabies and are made by the female scabies mite in the process of laying eggs.

(Table continued)

TABLE 3.28 *(Continued)*

Lesions	Description of Lesions
Primary lesions due to vascular pathology	
Petechiae	These are small (1–2 mm), blood-filled macular lesions that do not blanch on pressure. They arise due to minor haemorrhages in the skin.
Purpura	These are maculopapular lesions formed due to subdermal bleed and are 0.3–1 cm in size. They do not blanch on pressure.
Ecchymosis	Subdermal bleed >1 cm in size.
Telangiectasia	These are caused by dilatation of superficial blood vessels and are between 0.5 and 1 mm in diameter.
Secondary skin lesions	
Atrophy of the epidermis or dermis	Skin looks shiny and shows fine wrinkles on pressing between the finger and thumb.
Erosion	It is a partial loss of epidermis. It heals without scarring.
Excoriation	Scratch mark associated with pruritic disorders such as scabies and atopic eczema.
Fissure	Fissure is a linear slit in the skin due to loss of epidermis and dermis. It is often very painful. It is characteristically seen in intertrigo and eczema.
Scales	Scaling of the skin surface indicates an abnormality of the process of epidermal keratinisation. Scales are seen when imperfectly keratinised cells stick together in clumps. They may be small as in dandruff or large as in psoriasis. Scales must be distinguished from crusts (scabs), which are dried exudates.
Crusts/scab	Crusts are dried exudates. They are seen in cases with chicken pox. Crusts may be red due to haemorrhage, yellow-green due to pus or honey coloured due to serum.
Sinus	A small opening in a cavity through which it drains out.
Scar	Replacement of the injured tissues by fibrous tissues. It is seen after the healing of the wounds.
Ulcer	It is a discontinuity in the full thickness of the epidermis.
Lichenification	Thickening of the epidermis with the lesion elevated from the surface. This condition is seen in chronic irritation or inflammation. There is diffuse thickening of the skin with hyperpigmentation and increased skin markings.

skin formed due to deposition of fat-containing cells in the skin.

6. *Loss of sensations*: In Hansen's disease there is a loss of sensations over the lesions. Look for associated findings such as thickening of the peripheral nerves.
7. *Pleomorphism*: The lesions in chicken pox are pleomorphic, that is, the lesions are not uniform. Various stages of lesions are seen at a particular point of time. One can see all the stages such as vesicle and crusts at the same time. In measles, the rashes are uniform.
8. *Umbilication*: The centre of the papule is depressed. It is seen in lesions of chicken pox.
9. *Hyperkeratosis* occurs due to thickened stratum corneum. It is seen in children with vitamin A deficiency. Hyperkeratosis can occur anywhere in the body but more commonly around the elbows and knees. The skin is thickened to protect it from rubbing. When the skin is subjected to repeated friction, corns and calluses develop.

Neurocutaneous Syndromes

Neurocutaneous Markers. These are skin lesions associated with the nervous system (Table 3.29). The skin and the nervous system develop from the ectoderm. Hence, any defect in the ectodermal development presents with defects in both the skin and the nervous system. One should always look for lesions in the nervous system if any abnormality such as café au lait spots is noted in the skin (Fig. 11.2).

TABLE 3.29 Neurocutaneous Markers with Associated Conditions

Neurocutaneous Markers	Conditions
Café au lait spots	Neurofibromatosis
Subungual fibroma	Tuberous sclerosis
Ash leaf macule	Tuberous sclerosis
Adenoma sebaceum	Tuberous sclerosis
Shagreen patch	Tuberous sclerosis
Capillary haemangioma	Sturge–Weber syndrome
Telangiectasia	Ataxia telangiectasia Rendu–Osler–Weber syndrome
Haemangioma	Sturge–Weber syndrome
Nodules	Neurofibromatosis
Tubers	Tuberous sclerosis
Axillary freckling (Crowe's sign)	Neurofibromatosis
Hypopigmented patches	Tuberous sclerosis
Hyperpigmented patches	Neurofibromatosis
Tuft of hair on back	Spina bifida

Café au lait spots are milky coffee-coloured pigment patches seen on skin in patients with Von Recklinghausen's disease.

Hypomelanosis of Ito. It is a neurocutaneous syndrome, also known as incontinentia pigmenti achromians, with hypopigmented macules. It is associated with defects in others organs. There may be seizures, mental retardation, scoliosis and eye defects.

Infections of the Skin

Impetigo occurs due to the infection of superficial layers of skin by streptococci or staphylococci. It appears as small thin-walled vesicles that may rupture rapidly, leaving superficial ulcers (Fig. 3.36). It may be covered with bright yellow crusts (non-bullous impetigo) or may appear as large blisters (bullous impetigo). *Ecthyma*, also called 'deep impetigo', is caused by similar infection that spreads deep into dermis.

Boils or furuncles are the results of infection of hair follicle and its surrounding tissue. These begin as deep-seated inflammatory follicular nodules that may turn into pustules. These are common in malnourished children.

Carbuncles are formed due to an infection spreading to the contiguous follicles. Predisposing conditions are diabetes, malnutrition and prolonged steroid therapy.

Cellulitis is an infection of deep dermis and subcutaneous tissue. It manifests as red tender swelling with ill-defined border.

Erysipelas occurs due to an infection of superficial layer of the dermis by streptococci. It manifests as sharply defined, slightly elevated, tender erythematous area.

Lupus vulgaris arises due to an infection by mycobacterium tuberculosis in children with moderate or high degree of immunity. It manifests as single or multiple, erythematous, irregular, indurated plaques. This is associated with ulceration in some parts and scarring in other parts. This lesion extends slowly and irregularly at the periphery.

Scrofuloderma results from the rupture of the skin due to the underlying tuberculous infection of lymph nodes, bones and joints. The lesion consists of single or multiple sinuses with undermined edges. It may be associated with thin yellow pus discharge.

Typical Distribution and Associated Findings

The clinician should note the distribution of the skin lesions. Typical pattern of distribution often gives valuable information helpful in diagnosing the condition. One should also look for associated findings such as thickening of the peripheral nerves, which is seen in leprosy (Hansen's disease). Following points should be considered while assessing the pattern of distribution:

- Whether the lesions are symmetrical (both sides of the body show equal distribution of lesions) or asymmetrical. Symmetrical lesions are usually associated with a systemic cause.
- Whether the lesions are confined to the exposed parts of the body. This is often seen in lesions attributed to the sunlight (photodermatitis), insect bite, allergens such as dust, and phototoxic reactions to drugs such as sulphonamides, griseofulvin, psoralens and chlorpromazine. In solar dermatitis, itching and erythema develop within few hours after exposure to the sunlight.
- Whether lesions are more on the flexor or extensor aspect. Atopic dermatitis is commonly seen on the flexor aspect. The skin lesions of scabies are usually confined to the web of fingers, axilla and groin. In infants, the lesions can occur on the scalp as well.
- Whether the lesions are centrifugal or centripetal in distribution. Peripheral lesions present on the limbs are said to be centrifugal. When the lesions are more on the trunk, the lesions are said to be centripetal. The eruptions of chicken pox and maculopapular lesions of scrub typhus are usually centripetal in distribution. The lesions of erythema multiforme are centrifugal in distribution. The butterfly rash associated with systemic lupus erythematosus is usually seen on the face. Infantile eczema is seen on the cheeks.
- Whether the lesions are confined to hairy parts. Hairy parts, particularly of the head and pubis, are subject to troublesome infestations by minute insects and mites, such as chiggers and lice.
- Whether the lesions are localised to a specific area. This may be due to contact dermatitis in that area.

NAILS

Nails grow at a rate of 2–5 mm per month in the fingers and half that rate in toes. Growth rate of the nails is maximum in the childhood and decreases with age. Hence, any lesion in the nail can give a clue to the time of occurrence of the insult. Parts of a normal nail are illustrated in Fig. 3.40. Changes in nails can be due to local cause or secondary to systemic disorders. Nails are absent in nail-patella syndrome. Nephrotic syndrome is frequently associated with this condition.

Morphological Appearance

The external appearance of the nail varies with the underlying clinical condition.

The clinician should note the abnormal morphological appearance of nails. This can help him or her to diagnose the associated conditions.

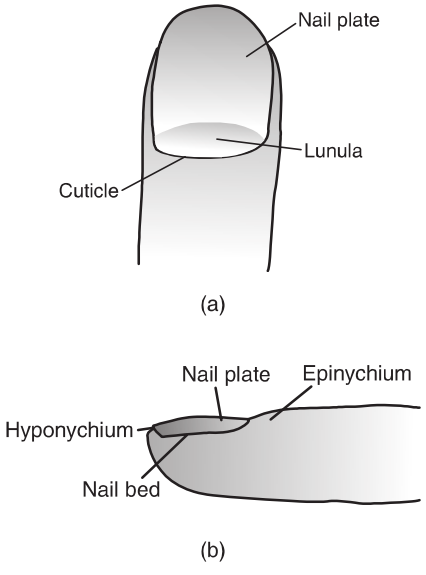


FIGURE 3.40 Parts of nail. (a) Dorsal view. (b) Lateral view.

Some of these criteria are as follows:

- Platynychia—the normal curve of the nail is lost and the nail becomes flattened. It is seen in chronic iron deficiency anaemia.
- Koilonychia—it is seen in patients with iron deficiency anaemia. The nails are typically spoon shaped, soft and brittle.
- Brittle nails—the nails are easily broken. Such nails are seen in patients with PEM and in old age.
- Absent nails—nails are absent in ectodermal dysplasia.
- Beau's lines are transverse ridges in the nails. They are seen in severe illness or malnutrition due to temporary stoppage of nail growth.
- Mees' lines are solitary transverse bands in the nail. They are seen in renal failure, chemotherapy and arsenic poisoning.
- Onycholysis is loosening or separation of nail from its bed. It is seen in trauma, psoriasis and thyrotoxicosis.
- Paronychia is the redness of the skin around the nail. This refers to the infections around the nail.
- Pitted nails are seen in psoriasis, eczema and alopecia areata.
- Discolouration of nail plates is seen in psoriasis.
- Splinter haemorrhage—this refers to the haemorrhage under the nail. It is seen in infective endocarditis, trauma, rheumatoid arthritis, collagen vascular diseases and trichinosis.
- Quinke's sign—it is seen in aortic regurgitation. There is blanching and refilling of the vessels in the nail bed.

Colour

The colour of the nails depends on the blood flow, haemoglobin content, form of haemoglobin and various other factors. Many conditions are associated with colour changes in the nails. Some of these are discussed in Table 3.30. Sometimes, colour changes are seen in only a part of the nails (Table 3.31).

TABLE 3.30 Colour Changes in the Nail and Associated Conditions

Features	Appearance	Associated Conditions
White nails (leukonychia)	Partial or total white discolouration	Hypoalbuminaemia—liver failure, nephrotic syndrome and protein-losing enteropathy
Pallor	Pale nails	Anaemia, shock, vascular compromise (obstruction to blood supply) etc.
Yellow nails	Yellowish colour seen better by blanching the nail bed by applying mild pressure over the tip of the nail	Jaundice Yellow nail syndrome---yellow nails, sinusitis, bronchiectasis and agammaglobulinaemia
Blue nails	Cyanosis	Cyanotic heart disease, exposure to cold and vascular obstruction
	Bluish discolouration of lunulae	Wilson's disease and argyria
Green nails	Partial or total green discolouration depending upon the severity	Pseudomonas infection
Terry's nails	Distal half is brown or red, proximal half is white in colour and lunula is absent	Cirrhosis and chronic renal failure
Red nails	Red discolouration all over the nail	Carbon monoxide poisoning
Mee's lines	Solitary white transverse bands above the lunula	Renal failure and arsenic poisoning
Beau's lines	Multiple unpigmented transverse ridges in the nail plate	Malnutrition, trauma and infection
Muechrcke's lines	White lines parallel to lunula separated by normal pink band in between	Hypoalbuminaemia due to cirrhosis and protein losing enteropathy

HAIR

The hair grows in a cyclic pattern where the growth phase (anagen phase), catagen phase and telogen phase alternate. The rate of growth varies with region and person and is also different for hair in different areas in the same person. For example, scalp differs

TABLE 3.31 Colour Change in a Part of Nail

Colour	Conditions
White or yellow nails	Onycholysis
Bright red nails	Fresh haematoma
Dark red nails	Old haematoma
Splinter haemorrhages	Infective endocarditis

TABLE 3.32 Typical Hair Changes Associated with Certain Conditions

Condition	Hair Changes
Preterm infants	Fine, woolly hair on the scalp Lanugo hair—fine, non-pigmented hair on the body and face that is lost within a few days of birth
Term infants	Silky, long and dark scalp hair
Kwashiorkor	Sparse, dry, hypopigmented, thin, brittle, lustreless and easily pluckable hair Flag sign—alternate bands of pigmented and depigmented hair
Tinea capitis or ring worm of the scalp	Loss of hair/scaling of the scalp
Congenital ectodermal dysplasia	Hair may be absent
Hypothyroidism	Dry, thin, lustreless, brittle and coarse hair Low hairline on the forehead
Kinky hair disease	Stubby, sparse, white and kinky hair Hairs appear normal at birth
Ataxia telangiectasia	Premature greying of hair
Homocystinuria	Fine, fair, friable hair easily removed by brushing

from body. Examination of hair gives clue to various disorders (Table 3.32).

Texture

The texture refers to the diameter of the hair in the body. The hair texture varies from individual to individual and also between different parts of the body in the same person. Different types of hair textures are as follows:

- Fine hair texture—small diameter
- Coarse hair texture—large diameter. This is the strongest type of hair
- Normal texture—medium diameter

Alopecia

Alopecia means partial or total loss of hair. It is seen in the following conditions:

- Zinc deficiency
- Polyendocrine deficiency syndrome (hypoparathyroidism, adrenal insufficiency and hypothyroidism)
- Fungal infections such as candidiasis and tinea capitis or ring worm of the scalp
- Vitamin D-dependent rickets type II

Alopecia Areata

Alopecia areata is characterised by a sudden loss of hair in patches over the scalp, eyebrows and eyelashes (Fig. 3.41). It may be seen in acrodermatitis enteropathica.

Hypertrichosis

Hypertrichosis is a condition in which excessive hair is present. The causes of hypertrichosis include the following:

- Bloom syndrome
- Drugs such as androgens, minoxidil diazoxide, penicillamine, phenytoin, anabolic steroids, acetazolamide, danazol, phenothiazines and oral contraceptives containing progestins
- Endocrine disorders such as Cushing's syndrome, hypothyroidism, precocious puberty, congenital adrenal hyperplasia, androgen-secreting tumours



FIGURE 3.41 Alopecia areata.

such as tumours of adrenal glands or ovaries, polycystic ovarian disease and male pseudohermaphroditism
- Foetal alcohol syndrome
- Foetal hydantoin syndrome
- Genetic disorders such as mucopolysaccharidosis

Hypotrichosis

Hypotrichosis is a condition characterised by decreased amount of hair on the body. Possible causes of this condition include the following:

- Hepatic failure
- Testicular atrophy
- Klinefelter's syndrome

Synophrys

In this condition, the eyebrows blend with each other in the midline. This is seen in patients with Cornelia de Lange syndrome.

SPINE

The spine is formed by vertebral bones. The normal spine is convex anteriorly in the lumbar region (lumbar lordosis) and concave anteriorly in the thoracic region. The movements seen in the spine are flexion, extension, lateral flexion and rotation.

Deformities

The deformities in the spine may result from the defects in the spinal vertebra or as a compensatory mechanism to maintain a normal vertical posture. The compensatory deformities get obliterated by change of posture or lying down. Various types of spine deformities include the following:

- *Kyphosis* is forward bending of vertebral column (Fig. 3.42).
- *Gibbus* is an angular deformity due to structural deformity of the vertebra, which is caused by fracture.
- *Lordosis* is an exaggerated backward curvature of vertebral column. It is commonly seen in the lumbar region (Fig. 3.43).



FIGURE 3.42 Kyphosis.

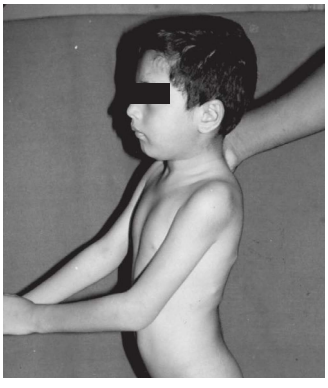


FIGURE 3.43 Lordosis.

- *Scoliosis* is a lateral curvature of vertebral column. It can be primary or secondary in origin.

Primary scoliosis occurs due to a structural defect in the vertebra and cannot be obliterated. It persists when the child bends down. It is seen in the following conditions:

- Poliomyelitis
- Muscular dystrophy
- Hemivertebra
- Idiopathic
- Osteogenesis imperfecta
- Marfan's syndrome

Secondary scoliosis is a condition where there are no bony deformities. The scoliosis disappears on lying down. It is of two types:

- Postural
- Compensatory—secondary scoliosis occurs due to compensatory phenomenon. For example, when one leg is short the child bends the spine laterally to maintain an erect posture. This type of scoliosis gets obliterated during sleep or lying down posture

VITAL SIGNS

Vital signs are the signs of life. These vary with age and in disease conditions. These include temperature, pulse, respiration and heart rate.

Temperature

The clinician can make a rough estimate of the body temperature by placing the dorsum of his or her hand over the neck of the child. It is not advisable to feel for the temperature at the peripheries, as it may be misleading in the presence of abnormal blood flow. For example, in shock, the peripheries are cold despite a normal core temperature.

The body temperature can be measured by using clinical thermometer. Core temperature is the actual temperature of the body, which is measured by a rectal thermometer inserted into the rectum. Ideally, the thermometer should be kept in the mouth or axilla for 3–5 minutes before it is taken out for reading.

Nowadays, plastic strips and digital ear thermometers are also available in the market to measure the body temperature.

Sites to Record Body Temperature

Various sites used to record body temperature are as follows:

- Oral cavity
- Axilla
- Rectum
- Groin (between the abdomen and the flexed thigh)
- Ear canal (tympanic membrane)

The clinician should remember that the rectal temperature is 1°F more than the oral temperature and the oral temperature is 1°F more than the axillary temperature.

Temperature Ranges

The temperature is usually recorded by placing a thermometer in the mouth. The body temperature depends upon various factors such as the presence or absence of infections, metabolic rate and endocrine abnormalities. The body temperature of a child can be classified as shown in Table 3.33.

Pulse

Pulse is the wave form generated by the left ventricular systole, which traverses the arteries in the peripheral direction. Thus, any abnormalities in the cardiac function or the arterial system are reflected in the pulse. Pulse should be palpated in all the peripheral arteries. It may be absent in lower limbs in coarctation of aorta. Pulse should be examined under the following headings:

- Rate
- Rhythm
- Character
- Volume
- Radiofemoral or radioradial delay
- Condition of the vessel wall

It is preferable to examine different arteries for different features of the pulse (Table 3.34). For example, volume of the pulse is best appreciated in carotid arteries, as they lie close to the heart.

TABLE 3.33 Temperature Ranges (Oral)

Temperature	Degree Centigrade	Degree Fahrenheit
Normal	36.6–37.2	98–99
Subnormal	<36.6	<98
Febrile	>37.2	>99
Hyperpyrexia	>41.6	>107
Hypothermia	<35	<95

TABLE 3.34 Characteristic Features of the Pulses

Feature	Artery	Findings
Rate	Radial artery	Bradycardia and tachycardia
Rhythm	Radial artery	Regular, irregular, regularly irregular or irregularly irregular
Character	Carotid artery	Slow rising, water hammer, pulsus alternans, etc.
Volume	Carotid artery	Normal, low or high
Radiofemoral delay	Radial artery Femoral artery	Usually, the femoral and the radial pulses are simultaneously palpable. In coarctation of aorta, there is a delay between the radial and femoral pulses
Vessel wall thickening	Radial artery	The vessel walls are thickened in atherosclerosis

Normal pulse rate at various ages are as follows:

Age	Beats/min
<6 months	120–160
6–12 months	110–120
1–5 years	95–110
6–12 years	80–110
>12 years	60–100

Respiratory Rate

The respiratory rate should be counted exactly by watching the chest or abdomen movements for 1 minute. The movements should be observed for at least 10 seconds. Table 3.35 lists the normal ranges of respiratory rate depending upon the age of the child.

Tachypnoea

Respiratory rate is increased in the following conditions:

- Anxiety, exertion, fever, hypoxia and acidosis
- Respiratory causes such as pneumonia, pulmonary oedema and adult respiratory distress syndrome
- Hysterical hyperventilation

TABLE 3.35 Normal Respiratory Rate at Various Ages

Age	Normal Respiratory Rate (Breaths/min)	Tachypnoea (Breaths/min)
Up to 2 months	30–50	>60
2–12 months	20–40	>50
12 months–5 years	20–30	>40
5–10 years	15–20	>30
>10 years	15–18	>30

Formula for calculating respiratory rate in children aged 6–20 years:
Respiratory rate = 31 – (0.8 × age in years)

Bradypnoea

Respiratory rate is decreased in the following conditions:

- Alkalosis
- Hypothyroidism
- Increased intracranial tension

Hyperpnoea

Increased depth of breathing is seen in the following conditions:

- Acidosis
- Hysterical
- Brainstem lesions

Blood Pressure

Blood pressure should ideally be recorded in all four limbs.

Cuff Size

Separate cuffs should be used for children of different ages. A cuff of the appropriate size covers two-thirds of the length of the arm on which it is tied, with the inflatable bladder covering the entire circumference of the arm with no overlapping. The size of the cuff varies according to the age of the child, as given in Table 3.36.

If a big size cuff is used, it may give a falsely low value. If the cuff is too small, it may give a falsely high value. Hence, a cuff of appropriate size should be used.

The cuff should be inflated rapidly and deflated slowly.

TABLE 3.36 Appropriate Cuff Sizes Used for Measuring the Blood Pressure at Various Ages in Children

Age	Dimensions of the Cuff (cm)			
	Cuff Size in the Arms		Cuff Size in the Legs	
	Width	Length	Width	Length
Newborn	2.5–4	5–9	6–9	17–18
Infants	4–6	10–13	8–9	20
1–2 years	6–9	13–18	12–14	25
2–8 years	7–10	17–20	14–16	28
8–12 years	8–12	20–24	16–18	30
Adolescents	12–14	22–26	18–20	32–38

Techniques to Measure the Blood Pressure in Children

1. *Auscultatory method (by using a sphygmomanometer)*: The cuff of the sphygmomanometer is tied in the arm and inflated. The cuff should be tied about 2.5 cm above the cubital fossa and should cover two-thirds of the arm. It should be inflated to about 20–30 mmHg above the level when the radial pulse is not felt. Now deflate the cuff. Auscultate the Korotkoff sounds over the brachial artery in the cubital fossa. For the lower limb, the stethoscope should be placed on the popliteal artery. The point at which the first Korotkoff sounds are heard is the systolic pressure. As the cuff is further deflated, the Korotkoff sounds get muffled and then disappear. The point at which the sounds start muffling (not disappear) is the diastolic pressure.
2. *Palpatory method*: Feel the radial pulse while the cuff is being deflated. The point at which the radial pulse reappears is the systolic pressure.
3. *Flush method*: This method is used in newborns and infants to measure the systolic blood pressure. Elevate the limb and hold it for some time. The cuff should be wrapped around the ankle or wrist. Now inflate the cuff of the sphygmomanometer above the expected systolic blood pressure. There will be blanching of the limb. The limb becomes pale. Now, bring down the arm and gradually deflate the cuff till the limb becomes pink again. The point at which there is flushing of the limb indicates the systolic blood pressure.
4. *Oscillometry method*: This is an invasive method and uses an oscillometer to detect the flow of blood in the radial or brachial artery.
5. *Doppler method*: This method uses the ultrasound Doppler to detect the flow in the radial or brachial artery.

Normal Blood Pressure in Children

The normal blood pressure in a child depends upon the age of the child. The blood pressure is low in newborn and infants. In older children, the blood pressure is more.

Age	Blood pressure (mmHg)	
	Systolic	Diastolic
Newborn	50–70	25–45
Up to 6 months	60–80	30–50
6 months–1 year	60–90	50–70
1–6 years	70–100	40–70
7–12 years	90–110	50–70

Formulae to Calculate the Expected Blood Pressure in Children

The following formulae are devised to approximately calculate the 50th percentile of systolic and diastolic blood pressures in children older than 1 year:

Systolic blood pressure = 90 + (2 × age in years)

Diastolic blood pressure = 55 + (2 × age in years)

Lower limit of systolic pressure (fifth percentile) = 70 + (2 × age in years)

Hypertension is said to be present if systolic and/or diastolic pressure are equal to or more than 95th percentile for that age and sex on at least three different occasions.

Pulse, Respiration and Temperature Relationship

A rise in temperature is associated with an increased heart rate. Therefore, an increase of 1°F in the body temperature results in an increase of the pulse rate by 10 beats per minute and respiratory rate by 4 beats per minute.

Pulse Pressure

Pulse pressure is the difference between the systolic and the diastolic blood pressures. The normal range of pulse pressure is 30–60 mmHg. A narrow pulse

pressure is seen in aortic stenosis and mitral stenosis. A wide pulse pressure is seen in patients with PDA and aortic regurgitation.

Mean Arterial Pressure

Mean arterial pressure is the product of the cardiac output and total peripheral resistance. The normal value of mean arterial pressure is 100 mmHg.

$$\text{Mean arterial pressure} = \text{diastolic pressure} + \text{1/3 of pulse pressure}$$

ANTHROPOMETRY

Anthropometry is the measurement of the body. It includes measurement of the following parameters:

- Weight
- Length, if the child is less than 2 years old or bed ridden
- Height, if the child is more than 2 years old
- Crown-rump length
- Head circumference
- Chest circumference
- Midarm circumference (This is constant in the age group of 1–5 years. There is an increase in the muscle mass and a decrease in the amount of fat. Hence, the measurement remains constant. In malnutrition there is wasting of muscles.)
- Skin fold thickness
- Upper segment to lower segment ratio
- Arm span

SYSTEMIC EXAMINATION

For detailed systemic examination, refer to separate chapters on each system.

The examination of the child should be done system-wise so that important findings are not missed. Depending upon the clinical presentation, preference should be given to a particular system. For example, if a child presents with paralysis of one side of the body, nervous system should be examined in detail. If the child presents with angina, cardiovascular system should be examined in detail, followed by examination of other systems. Involvement of one system affects the other. For instance, cardiac arrhythmias may be associated with thromboembolism, resulting in neurological deficits. Hence, it is important to examine all the systems.

The scheme of examination is detailed as follows.

Inspection

Observation of the child should start as soon as the child enters the examiner's room. Inspect the child after exposing the part of the body to be examined. Look for any pulsations or abnormal movements carefully.

Palpation

The hands of the examiner should be warm and dry. The findings of the inspection are confirmed by palpation. The child should be made comfortable prior to the examination.

The palpation can be done in the following ways:

1. Superficial palpation is done by placing the hand lightly on the part to be examined. Little or no pressure is applied while palpating.
2. Deep palpation is done by placing the hand on the part to be examined and applying pressure.
3. Bimanual palpation is used to palpate abdominal organs such as kidney where both hands are placed on the front and the back sides of the abdomen.

Thrill can be palpated over the stenosed arteries or an area of abnormal flow in the heart.

Percussion

Method: For percussion, the middle finger of the left hand is used as a pleximeter finger (Fig. 3.44). The volar aspect of this finger is placed on the part to be percussed so that there is no gap between the finger and that part. The back of the middle phalanx of the pleximeter finger is struck with the tip of the middle finger of the right hand. This movement should be at the wrist rather than at the elbow, and the percussing finger should strike the pleximeter finger perpendicularly. To facilitate this, terminal phalanx should be flexed at a right angle to the metacarpal



FIGURE 3.44 Method of percussion.

bone. The finger should be raised away from the pleximeter finger as soon as the finger strikes it. The character of the sound produced should be felt by the pleximeter finger. The clinician should always compare the percussion of the examined part with the corresponding part on the opposite side.

Percussion is done in the following ways:

- Direct percussion—using the index finger over the clavicle
- Indirect percussion—as described above
- Ausculto percussion—for detecting minimal ascites. With the child in knee–elbow position, place the stethoscope over the umbilicus. Now start percussion from the lateral part towards the umbilicus. Any change in the percussion note is observed

Auscultation

The sounds produced inside the human body may not be audible to ears. These sounds are better perceived by a stethoscope. Depending upon the condition suspected, either the diaphragm or the bell of the stethoscope should be placed on the chest for auscultation.

Low-pitched sounds are preferably auscultated using the bell and high-pitched sounds by using the diaphragm of the stethoscope.

Auscultation can be done in the following cases:

1. In a quiet child
2. Dynamic auscultation—usually the child is still when routine auscultation is done. In dynamic auscultation, the child is asked to do certain manoeuvres such as exercise, standing up and holding the breath during inspiration. Auscultation during or after these manoeuvres will change or unmask the findings

Precautions

The following precautions should be observed during auscultation:

- The child should be relaxed or lying down on the bed.
- The bell or diaphragm should not be cold.
- Surroundings should be quiet.
- The child should be explained about the examination.
- In a crying child, respiratory sounds are heard in between the cry. Cardiac examination is done while the child is sucking at the breast or sleeping.
- Always auscultate the front and the back.
- Ask the child to breathe deeply and regularly with open mouth.
- Do not give undue pressure or place the diaphragm too lightly on the body.
- There should be no gap between the stethoscope and the skin. If a gap is present, the rubbing of the skin against the diaphragm may produce crackling sound.
- The clinician should auscultate with the same stethoscope and avoid changing it often.

LYMPHADENOPATHY

Lymphadenopathy is defined as enlargement of lymph nodes due to inflammatory or non-inflammatory causes. There are about 500–600 lymph nodes in the human beings. These are distributed throughout the body and are found in clusters in underarms, groin, neck, chest and abdomen. The internal lymph nodes cannot be palpated easily and are present in thoracic and abdominal cavities. Sites of palpable lymph nodes and their drainage areas are given in Table 3.37. The important lymph nodes draining

TABLE 3.37 Sites of Palpable Lymph Nodes with Their Drainage Areas

Nodes	Site	Drainage Area
Head and neck		
Occipital	In the occipital region posterior to mastoid process at the base of the skull	Back of scalp
Preauricular	In front of tragus of the ears	Eyelids, conjunctiva, temporal region, pinna
Postauricular	Behind the ears over the mastoid process	External auditory meatus, pinna, scalp above the ear
Anterior cervical	Along the anterior jugular vein in front of the neck	Skin and superficial tissues of the front of neck
Superficial cervical	They lie along the external jugular vein superficial to the sternocleidomastoid muscle	Angle of jaw, skin over the lower part of parotid gland and lobe of ear; they drain into deep cervical lymph nodes
Deep cervical	They form a vertical chain along the course of internal jugular vein and receive lymph from all groups of regional lymph nodes	Jugulodigastric node—tonsil and tongue Jugulo-omohyoid—tongue
Posterior cervical	In the posterior triangle along the trapezius	Scalp and neck, skin of arms, pectoralis, thorax, cervical and axillary nodes
Submandibular	Underside of the jaw on either sides in the oral cavity	Tongue, submaxillary glands, lips, structures in the floor of the mouth, conjunctiva, mandibular teeth except central incisors
Submental	Just below the chin in the midline in the floor of the mouth	Central incisors and midline of lower lip, floor of the mouth, tip of the tongue, skin of cheek

(Table continued)

TABLE 3.37 *(Continued)*

Nodes	Site	Drainage Area
Supraclavicular	In the hollow above the right clavicle in the angle of the sternomastoid and clavicle	Part of thoracic cavity and abdomen, mediastinum, lungs, oesophagus
	In the hollow above the left clavicle (Virchow's node)	Most parts of body especially abdomen through thoracic duct
Upper limbs		
Axillary		
Lateral (brachial)	In the armpit medial and posterior to the axillary vessels	Upper limb
Central	At the base of the axilla	Receives afferents from lateral, anterior and posterior nodes
Medial (apical or subclavicular)	Partly posterior and partly superior to pectoralis minor muscle	Superior breast, mammary tail and thoracic wall; it also receives afferents from other group of axillary nodes
Anterior (pectoral)	Pectoral	Anterior chest wall, most of breast (central and lateral breast)
Posterior (subscapular)	Subscapular	Posterior chest wall, upper arm, lower posterior neck
Epitrochlear	Just above the elbow crease on the medial side of the body	Ulnar aspect of forearm and hand
Infraclavicular	Inferior to the clavicle	Receive lymph from superficial vessels around the cephalic vein
Lower limbs		
Inguinal superficial (horizontal, vertical) and deep	Inguinal region (groin)	Penis, scrotum, vulva, vagina, perineum, gluteal region, lower abdominal wall and lower anal canal
Femoral	In the upper inner thigh	Foot, leg, groin and genitals
Popliteal	Opposite to the knee	Legs and feet

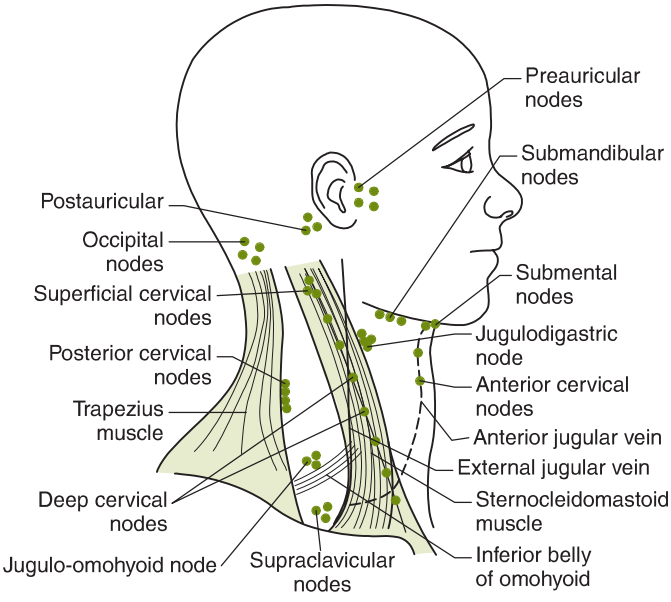


FIGURE 3.45 Lymph nodes in head and neck.

the regions of head, neck, thorax and extremities are as follows:

1. Head and neck (Fig. 3.45)
   - Occipital
   - Preauricular
   - Postauricular
   - Anterior cervical
   - Superficial cervical
   - Deep cervical—the jugulodigastric node is a deep cervical lymph node
   - Posterior cervical—they lie posterior to sternomastoid and in front of trapezius muscles
   - Submandibular
   - Submental
   - Supraclavicular
2. Thorax
   - Lymphatic drainage of the lungs is by hilar lymph nodes through subsegmental, segmental, lobar and interlobar lymph nodes
   - Mediastinal lymph nodes are present along the oesophagus and between the lung and diaphragm
3. Upper limbs
   (a) Superficial lymph nodes
   - Supratrochlear or epitrochlear lymph nodes are situated above the medial epicondyle of the humerus
   - Deltopectoral or infraclavicular lymph nodes are present between pectoralis major and deltoid muscles inferior to the clavicle

   (b) Deep lymph nodes
   - Axillary glands—anterior (or pectoral), posterior (or subscapular), medial (apical or subclavicular), lateral (brachial) and central
4. Lower limbs
   - Superficial and deep inguinal lymph nodes
   - Femoral lymph nodes
   - Popliteal lymph nodes

AETIOLOGY

Causes of lymphadenopathy are as follows:

1. Inflammatory and immunological causes
   - Bacterial—streptococcal and staphylococcal infection, brucellosis, tuberculosis, typhoid fever, plague and syphilis
   - Viral—infectious mononucleosis, cytomegalovirus, AIDS, rubella, measles, varicella and lymphogranuloma venereum
   - Fungal—histoplasmosis and coccidioidomycosis
   - Protozoal—malaria and toxoplasmosis
2. Connective tissue disorder
   - Rheumatoid arthritis
   - Systemic lupus erythematosus (SLE)
   - Serum sickness
3. Granulomatous disease
   - Sarcoidosis
   - Amyloidosis
4. Endocrine causes
   - Hyperthyroidism
   - Addison's disease
5. Drugs
   - After hydantoin therapy
   - Allopurinol
6. Storage diseases
   - Gaucher's disease
   - Niemann–Pick disease
7. Neoplasms
   - Primary—acute leukaemia, Hodgkin's and non-Hodgkin's lymphoma, chronic myeloid leukaemia, neuroblastoma and myeloproliferative disorders
   - Secondaries—due to primary in head, neck, lung, etc.
8. Miscellaneous
   - Histiocytic disorders—histiocytic necrotising lymphadenitis
   - Castleman disease

Terminologies used:

1. Generalised lymphadenopathy—involvement of more than two non-contiguous lymph node areas due to a systemic disease.
2. Localised lymphadenopathy—involvement of one lymph node area.
3. Persistent lymphadenopathy—persistence of lymphadenopathy for 3 months or more.
4. Significant lymphadenopathy—lymph node enlargement is seen in many non-specific conditions. The lymph node enlargement is considered significant if any of the following factors are present:
   - Size—inguinal nodes >1.5 cm diameter, cervical and axillary nodes >1 cm diameter, epitrochlear nodes—any size
   - Site—multiple sites
   - Matted nodes
   - Nodes which are red/tender/ulcerated
   - Associated with focus of infection
   - Associated with systemic signs and symptoms

CLINICAL EVALUATION

The child usually presents with swelling in neck or axilla which may or may not be associated with pain. A detailed history to find the cause should be followed by physical examination in such cases. The following points should be noted during history taking of the child for lymphadenopathy:

- Infective causes are common in younger age group whereas malignancy is common in older age group
- SLE is common in females
- Duration—short duration in infections
- Constitutional symptoms—fever, weight loss and fatigue
- H/o fever—infections, collagen vascular diseases
- Pel–Ebstein type of fever (Hodgkin's lymphoma)
- H/o night sweat—lymphoma
- H/o weight loss—tuberculosis, malignancy
- H/o pain—painful nodes are seen in infection

and inflammation; painless nodes are seen in malignancy
- H/o bleeding gums—leukaemia
- H/o bony tenderness—leukaemia
- H/o intolerance to heat and diarrhoea (hyperthyroidism)
- H/o joint pain in juvenile rheumatoid arthritis or inflammation of joint (the nodes proximal to the joint are enlarged)
- H/o drug intake—phenytoin, cephalosporins, penicillin, sulfonamides and allopurinol
- H/o contact with communicable diseases such as tuberculosis

EXAMINATION OF LYMPH NODES

The lymph nodes are palpated by the pads of index and middle fingers with gentle but firm pressure and moving the overlying skin in circular motions. These should be described in terms of their location, size (in cm), number (single/multiple), surface (rubbery/smooth), texture (discrete/matted), consistency (soft, firm, hard, pleomorphic), mobility (mobile/fixed), temperature and tenderness. The skin over the lymph node should be examined for signs of inflammation and sinus formation (tuberculosis). The head and neck lymph nodes are usually palpated together. Method of palpating lymph nodes at various sites is given in Table 3.38 (see also Fig. 3.46). Some specific characters of lymph nodes are given in Table 3.39.

TABLE 3.38 Method of Palpating Lymph Nodes

Lymph Nodes	Method of Examining
Head and neck	
Occipital	Palpate behind the ear posterior to mastoid process at the base of the skull
Preauricular	Palpate by rolling the fingers in front of the ears against the maxilla
Postauricular	Palpate by rolling the fingers behind the ears
Submandibular	Palpate bimanually in the submandibular area as the node is pushed up and inside
Submental	Palpate in the submental area against the mylohyoid muscle using the index finger
Superficial cervical	Glands of anterior triangle should be examined bimanually from behind
Deep cervical	The deep cervical nodes are palpated one at a time by gently flexing the head towards the side on the side of palpation. The fingers are hooked beneath the anterior edge of the sternomastoid muscle and rolled over the deep muscles along the carotids
Posterior cervical	Glands of posterior triangle should be examined bimanually from front along the anterior margin of trapezius
Supraclavicular	Roll the fingers gently behind the clavicles. The gland may be palpated when the child coughs during examination
Upper limbs	
Axillary (anterior, medial, lateral and central)	These are examined while standing in front of the patient by inserting the fingers in the axillary vault with the patient's arm slightly abducted. The arm on the side of examination is supported with the examiner's hand. The right-sided axilla is palpated with left hand and vice versa • The anterior axillary nodes are palpated on the posterior surface of pectoralis major that forms the anterior axillary fold • The apical nodes are palpated deep into the axilla by slightly depressing the patient's shoulder • The medial group is palpated against the upper lateral chest wall • The lateral group is palpated against the upper medial humerus
Axillary posterior	These are examined while standing behind the patient. The patient's shoulder is slightly abducted and his hand is placed over his opposite shoulder. The right-sided nodes are palpated with right hand and left-sided nodes with left hand along the anterior surface of posterior axillary fold which is formed by latissimus dorsi
Epitrochlear	These are palpated in a partially flexed elbow
Lower limbs	
Inguinal	Horizontal group is palpated below the inguinal ligament
Popliteal	These are palpated bimanually with the knees flexed and the limb muscles relaxed



(a)



(b)



(c)



(d)



(e)

FIGURE 3.46 Methods of palpating lymph nodes. (a) Anterior axillary. (b) Medial axillary. (c) Lateral axillary. (d) Anterior cervical. (e) Posterior cervical.

TABLE 3.39 Characteristics of Lymph Nodes

Character	Conditions
Soft	Infections/inflammatory conditions
Firm	SLE, Hodgkin's lymphoma
Hard	Malignancy lymphoma
Stony hard	Malignancy, metastases
Firm, rubbery	Hodgkin's lymphoma
Fluctuant	Suppurative
Shotty (small, mobile, discrete, hard and round; resembling lead pellets)	Viral infections

INVESTIGATIONS

1. Complete blood count
   - Leucocytosis in pyogenic infections
   - Lymphocytosis in tuberculous infection
   - RBC count—anaemia in leukaemia
   - Platelet count—thrombocytopenia
2. Investigations for causative factors
   - Tuberculosis—Mantoux test, chest X-ray and lymph node biopsy
   - Infectious mononucleosis—Paul–Bunnell test
   - Malignancy—bone marrow aspiration or biopsy (blast cells in leukaemia), fine needle aspiration cytology and excision biopsy

SURFACE AREA

Body surface area (BSA) is the measure of the area of the body, expressed in square units. Table 3.40 gives the approximate surface area in children of various ages.

Surface area can be calculated by the following formulae:

1. Mosteller formula:

$$\text{BSA}(m^2) = \sqrt{\frac{\text{weight (kg)} \times \text{height (cm)}}{3600}}$$

This is the most commonly used formula.

2. Dubois and Dubois formula

$$\text{BSA } (m^2) = 0.20247 \times \text{height (m)}^{0.725} \times \text{weight (kg)}^{0.425}$$

TABLE 3.40 Normal Body Surface Area in Children of Various Ages

Age	Body Surface Area (m^2)
At birth	0.25
3 months	0.3
1 year	0.45
2 years	0.5
3 years	0.6
6 years	0.75
9 years	0.9–1.07
10 years	1.14
12–13 years	1.33
Adult male	1.9
Adult female	1.6

Variation of Dubois and Dubois formula:

$$\text{BSA } (m^2) = \text{weight (kg)}^{0.425} \times \text{height (cm)}^{0.725} \times 0.007184$$

3. Haycock formula—this formula has an advantage that it can be used for newborns.

$$\text{BSA } (m^2) = 0.024265 \times \text{height (cm)}^{0.3964} \times \text{weight (kg)}^{0.5378}$$

4. Gehan and George formula:

$$\text{BSA } (m^2) = 0.02350 \times \text{height (cm)}^{0.42246} \times \text{weight (kg)}^{0.51456}$$

5. Boyd formula:

$$\text{BSA } (m^2) = 0.0003207 \times \text{height (cm)}^{0.3} \times \text{weight (g)}^{0.7285 - (0.0188 \times \log_{10} \text{weight (g)})}$$

6. Another formula:

$$\text{BSA } (m^2) = \frac{4 \times \text{weight (kg)} + 7}{90 + \text{weight (kg)}}$$

7. Another simple formula for children weighing 3–30 kg is

$$\text{BSA } (m^2) = \frac{(\text{weight (kg)} + 4)}{30}.$$

SIGNIFICANCE

The surface area of children is useful in assessing various factors as follows:

- Regulation of body temperature

- Basal metabolic rate
- Blood volume
- Cardiac index = cardiac output/BSA
- Renal clearance
- Estimation of the dosage of drugs to be given
- Digestion
- Chemotherapy

A good clinical examination will result in a good provisional diagnosis, thereby minimising the extent of investigations to be performed.

CHAPTER 4

Growth and Development

Growth is increase in size of the organs and body. It is a quantitative change and refers to physical maturation of the body.

Development is maturation of functions. It is a qualitative change and refers to functional or physiological maturation of the body. It is related to the acquisition of skills and a variety of competences for normal functioning of the individual.

GROWTH

Growth is a continuous process and extends through the prenatal and postnatal periods to maturity (Table 4.1). Physical maturation is complete by 18 years of age in females and by 20 years in males. Emotional development is a continuous process and continues in the adult life.

PRENATAL GROWTH

Monitoring

Monitor the crown-rump length in utero by repeated measurements using ultrasound. The foetal age is calculated by measuring the length of the foetus and not the weight. From 20th week of gestation onwards, vertex to the heel length should be measured. This is approximately five times the gestational age in months. During the second and third trimesters, the biparietal diameter and the length of the femur are used to estimate the gestational age.

Total maternal weight gain during pregnancy with a single conceptus should be at least 10 kg. The rate of weight gain is about 1 kg in the first trimester and 5 kg each in the second and third trimesters.

TABLE 4.1 Periods of Growth

Terminology	Period
Prenatal period	
Ovum	Ovulation to 14 days
Embryo	15 days–8 weeks
Foetus	9 weeks to birth
Perinatal period	22 weeks of gestation to 7 days after birth
Postnatal period	
Newborn	First 28 days after birth
Infancy	First year
Toddler	1–3 years
Preschool child or early childhood	3–6 years
School-age child or middle childhood	6–10 years (girls) 6–12 years (boys)
Adolescent • Prepubescent or late childhood • Pubescent • Postpubescent	 10–12 years (girls) 12–14 years (boys) 12–14 years (girls) 14–16 years (boys) 14–19 years (girls) 16–20 years (boys)

Weight gain more than 2 kg/month may be due to toxaemia of pregnancy which is associated with foetal mortality. Stationary or decreasing weight is a feature of intrauterine growth retardation (IUGR) or intrauterine death.

Haase Rule to Calculate the Foetal Age

First 5 lunar months	Age (in months) = √Length (in cm)
Next 5 lunar months	Age (in months) = Length (in cm)/5

Factors Affecting Prenatal Growth

Prenatal growth depends upon a number of intrauterine factors. These factors have both positive and negative influence on the growth and development of the baby. One should be aware of these factors so that they can be identified early and corrected.

Favourable Factors

1. Obstetric factors
   - Good weight gain (10 kg)
   - Placental adequacy
   - Interval between pregnancies >2 years
2. Maternal factors
   - Habits—good diet, mild exercise and meditation
   - Drugs—iron and folic acid
   - Conditions—healthy mother, free from illness
3. Hormones
   - Thyroxine
   - Insulin
   - Glucocorticoids
4. Foetal growth factors
   - Insulin-like growth factor (IGF-1 and 2)
   - Epidermal growth factor (EGF)
   - Transforming growth factor (TGF-α)
   - Platelet-derived growth factor (PDGF)
   - Fibroblast growth factor (FGF)
   - Nerve growth factor
5. Hereditary and genetic factors
   - Tall parents
   - Good parental traits
6. Healthy parents

Unfavourable Factors

The following conditions predispose to preterm or small-for-gestation babies:

1. Obstetric factors
   - Poor weight gain (<10 kg)
   - Placental insufficiency
   - Placenta praevia
   - Pregnancy-induced hypertension
   - Multiple pregnancies
   - Eclampsia
   - Interval between pregnancies <2 years
2. Maternal factors
   - Habits—addiction to alcohol, smoking and drug abuse
   - Drugs—teratogenic drugs such as thalidomide
   - Infections—urinary tract and intrauterine infections
   - Diseases—diabetes, heart diseases, anaemia and chronic renal failure
3. Foetal growth inhibitory factors
   - TGF-β
   - Müllerian inhibitory substance
   - Inhibin/activin
4. Hereditary and genetic factors
   - Inherited mental and physical defects
   - Chromosomal disorders

POSTNATAL PERIOD

The growth of the infant after delivery is influenced by various factors. One should know the normal rate of growth in order to monitor the growth. Any deviation from normal should be identified early and assessed for the causative factors.

Factors Affecting Postnatal Growth and Development

The following factors affect the postnatal growth and development of the child.

1. Age—the rate of increase in height is more in children as compared to adults.
2. Sex—girls have a growth spurt earlier than boys, but their final height and weight are usually less as compared to boys.
3. Race—growth is slow in certain races. Skeletal maturity occurs earlier in Blacks as compared to Whites.
4. Biorhythm—growth of girls resembles that of their mothers.
5. Hereditary (genetic) factors—children with chromosomal disorders like Down's syndrome and Turner's syndrome will be short.
6. Seasonal variation—the rate of growth is high in spring and low in summer.
7. Antenatal factors—intrauterine factors like feto-foetal transfusion and materno-foetal transfusion result in decreased blood supply to the growing foetus and predispose to IUGR. When the insult occurs to the growing foetus in early pregnancy, there is a decrease in the number of cells in the body. Thus, the growth potential will be decreased. Some of these children may not be able to achieve the normal growth and consequently have short stature.
8. Natal factors—severe birth asphyxia results in diffuse brain damage. Such children manifest slow growth.
9. Nutritional factors—children with malnutrition and minerals and vitamins deficiency suffer from growth retardation.
10. Hormonal factors—adequacy of hormone levels has a positive influence on growth and development.
    - Thyroxine is required for skeletal maturation. In children with thyroxine deficiency, growth retardation and mental retardation are seen.
    - Growth hormone (GH) facilitates linear growth. In children with growth hormone deficiency, the height is decreased.
11. Environmental factors
    - Infections—recurrent infections result in increased metabolic needs, and thereby predispose to growth retardation. Malnutrition and growth retardation are common in children with immunodeficiency.
    - Trauma to growing part of bones—injury to the epiphysis may result in growth retardation.
    - Illness—if the child suffers from conditions like anaemia and chronic systemic illness, the growth is affected.
12. Social factors:
    - Socioeconomic class—the children in upper socioeconomic class are usually taller than those in lower socioeconomic class. They are also less likely to suffer from infections because of proper hygienic living conditions.
    - Cultural habits—infant feeding practices, child rearing practices and various food fads prevalent in the community have a bearing on the postnatal growth and nutrition of the child.
    - Education of parents—educated parents, especially mothers, are able to give better care to their children than illiterate parents.
    - Education of the child—schooling at appropriate age will have a positive influence on growth. Lack of schooling or inadequate schooling will have an adverse effect on growth.
    - Psychological factors—lack of emotional support and insecurity are usually seen in children from broken families. These factors adversely affect the growth of the child. Responsible and intelligent parents are able to provide good care to the child.
    - Psychosocial factors—child abuse results in poor growth of the child.

RATE OF GROWTH

Rate of growth varies with age, sex, season and type of tissue.

Variation with Age

Growth is more rapid in the last 3 months of gestation and first 4–5 months after birth.

Age	Rate of growth
Birth to 2 years	Rapid
3–10 years	Slow
Puberty (12–14 years in girls and 14–16 years in boys)	Growth spurt
Adult	Almost zero

Variation with Gender

In girls, pubertal growth occurs earlier as compared to boys. Girls, therefore, attain their final height at an earlier age, though their final height and weight are usually less than the boys.

Variation with Season

The rate is more during spring and less in autumn.

Variation with Type of Tissue

The rate of growth depends upon the type of the tissue (Fig. 4.1). Different tissues in the body grow at different rates, described as follows:

- General body growth—there are two growth spurts in the general body growth. First, rapid growth occurs in the first 2 years of life. The weight of the body triples the birth weight at the end of first year and quadruples at the end of the second year. The second growth spurt occurs in the pubertal period.
- Brain growth—the brain grows at a rapid rate in the third trimester and first year of life.
- Gonadal growth—the maximum growth occurs in the pubertal period.
- Lymphoid tissue growth—the rapid growth of the lymphoid tissue occurs in the mid-childhood.

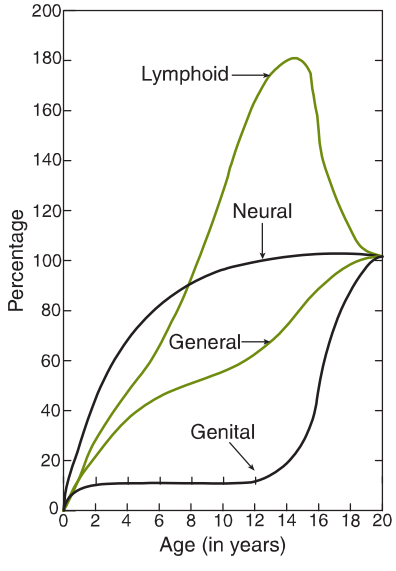


FIGURE 4.1 Rate of growth of different tissues in the body.

CATCH-UP GROWTH

Children who weigh below the expected due to starvation or undernutrition start gaining weight rapidly with adequate diet, so that they catch up with other normal children. This is known as catch-up growth. The growth of a child is slow during periods of starvation. When proper nutrition is supplied, the rate of growth is more in such children as compared to other children of the same age, till the child regains the normal weight expected for the age. The ultimate catch-up growth depends upon the duration of illness and cessation of growth. If the duration is too long, the catch-up growth does not achieve normal height and weight for age.

ASSESSMENT OF GROWTH

Physical growth is the sensitive indicator of the child's nutritional status. It is important to assess the growth of a child so that any deviation from normal can be identified and corrected early. Assessment of physical growth is done by evaluation of the following factors.

Anthropometry

Anthropometry means measuring the human body. Evaluation of growth is done by measuring the following:

- Weight
- Stature (length/height)—in children less than 2 years of age, supine length should be measured by an infantometer. In older children, standing height should be measured by means of a stadiometer

- Head circumference
- Chest circumference

These are discussed in detail in the section *Anthropometry*, page 98.

Dental Age

Teeth develop from ectoderm. At birth, the maxillary and mandibular centres are absent.

Primary Teeth

Primary teeth or deciduous teeth form in dental crypts which arise from dental laminae (band of epithelial cells). The primary dentition comprises 20 teeth. There are four incisors (two central and two lateral), two canines and four molars in each jaw.

Eruption of Primary Teeth. The teeth in the upper jaw erupt earlier than the lower jaw, except lower central incisors. The deciduous teeth usually erupt in the following order:

1. Lower central incisors erupt first followed by upper central and then upper lateral incisors
2. Lower lateral incisors
3. First deciduous molar
4. Canine
5. Second deciduous molar

The age of appearance is summarised in Table 4.2.

Variations in Primary Dentition. Although the eruption of teeth follows a developmental pattern, individual variation is considerable. Rarely, one or two teeth are prematurely present at birth. These supernumerary teeth are usually loosely held and easily removed. The tooth buds of the deciduous teeth are readily evident in the gums of the young infant. Eruption of the deciduous teeth may be delayed normally until the end of the first year. Further delay may occur in infants with hypothyroidism, hypopituitarism and vitamin A and vitamin D deficiencies. Early eruption of primary teeth is seen in hyperthyroidism. All 20 deciduous teeth should be present before the end of the third year.

TABLE 4.2 Eruption of Deciduous Teeth

Age	Eruption
Birth	Nil
6–8 months	Central incisors
By 10 months	Lateral incisors
12–15 months	First molars
15–21 months	Canine
21–24 months	Second molars

Loss of Primary Dentition. The lower central incisors are usually the first deciduous teeth to be lost. The last deciduous teeth are lost by about 12 years of age. During the preschool period, the presence of spaces between the anterior deciduous teeth is normal. Prolonged retention of deciduous teeth may be noted in pycnodysostosis and cleidocranial dysostosis.

Permanent Teeth

The permanent teeth comprise 32 teeth. There are four incisors, two canines, four premolars and six molars in each jaw.

Eruption of Permanent Teeth. The permanent teeth usually erupt in the following order:

Age (years)	Eruption
6	First molars
7–8	Central and lateral incisors
9	First premolar
10–11	Second premolar
11–12	Canines
12–13	Second molars
17–22	Third molars (wisdom teeth)

The first (sixth year) molars of the permanent dentition erupt behind the baby molars. Although the eruption of teeth follows a developmental pattern, individual variation is considerable. During the first year after their eruption, the permanent teeth appear relatively large and may be irregularly spaced and aligned. With further growth of the face, however, the teeth become proportionate to face.

Bone Age

Assessment of bone age is based on the time of appearance of ossification centres and the epiphyseal–diaphyseal union. The epiphyses of different bones appear at different times. This knowledge can be used

to assess the bone age and is helpful in evaluation of children with short stature. The shaft of the bone ossifies earlier than the ends.

The bone age estimation takes into consideration the following factors:

1. Time of appearance of epiphyses—assessment of bone age postnatally is based on the number, shape and size of epiphyseal centres and the time of fusion of epiphyses.
2. Progress of maturity—the sequence of changes in size, shape and density of the ends of bones which takes place is identical in all individuals.
3. Time when all the epiphyses are present.

Appearance of Ossification Centres

Intrauterine Period. There is a wide variation in appearance of epiphyseal centres in the foetus. The earliest epiphyseal centres to appear are os calcis and talus bones between 22 and 26 weeks of gestation. The distal epiphysis of the femur and the proximal epiphysis of tibia are present in a full-term normal newborn at birth.

Neonatal Period. X-ray of knee or ankle and foot should be taken in a newborn to assess the bone age (Table 4.3). At birth, X-ray of knee shows appearance of epiphyses at the lower end of femur and the upper end of tibia. A full-term newborn usually has the following five radiologically demonstrable ossification centres at birth:

- Epiphysis of the distal end of femur
- Proximal epiphysis of the tibia
- Cuboid
- Talus
- Calcaneum

Infancy and Childhood. By the age of 6 months, ossification centres for the carpal bones, that is, capitate and hamate, appear. It is a useful guide to remember that the number of ossification centres in wrist is equal to the age in years plus one.

$$\text{Number of ossification centres in wrist} = \text{Age (years)} + 1$$

Thus, a child aged 2 years should have three ossification centres. From 1 to 8 years, bone age is determined by examining carpal bones in the X-ray of the left wrist (Table 4.4).

TABLE 4.3 Radiological Evaluation of Bone Age at Various Ages

Age	X-ray	Finding
Newborn	Knee, ankle and foot	Five ossification centres • Epiphysis of the distal end of femur • Proximal epiphysis of the tibia • Cuboid • Talus • Calcaneum
6 months	Wrist of the left hand	Ossification centres for the carpal bones, i.e., capitate and hamate
3–9 months	Shoulder	Humerus upper end
1 year	Knee	Lower end of the femur and upper end of tibia
3 years	Wrist	Metacarpals and phalangeal centres
1–12 years	Wrist of the left hand	Up to 8 years—number of carpal bones
		8–12 years—distal ulnar epiphysis 8–9 years—girls 10–12 years—boys
12–16 years	Elbow	Distal end of humerus—lateral epicondyle
	Hip	12 years—lesser trochanter 16 years—iliac crest

TABLE 4.4 Number of Ossification Centres in Wrist According to Age

Age (years)	Number of Ossification Centres in the Wrist
1	2 (capitate and hamate)
2	3
3	4
4	5
5	6
6	7
7	8

The number of carpal bones and their appearance are noted. X-ray of the left hand is taken because most people are right-handed and are prone to injuries which can give abnormal shadows. Wrist is an area where multiple bones can be seen together. Also, this part can be visualised easily with low-radiation X-rays.

TABLE 4.5 Age of Appearance of Ossification Centres

Age (years)	Part of the Bone Ossified
5	Head of radius, trapezoid, scaphoid
6	Lower end of ulna, trapezium
6–7	Medial condyle of humerus
9	Olecranon
9–11	Trochlea of humerus
10–11	Pisiform
11	Lateral condyle of humerus
13	Separate centres in triradiate cartilage of acetabulum
14	Crest of ileum Head and tubercles of ribs
15	Acromion
16	Ischial tuberosity
18–19	Inner end of clavicle

Between 12 and 16 years of age, X-ray of the elbow and hip (Table 4.3) is taken for assessment of bone age. Table 4.5 summarises the age of appearance of ossification centres in the human body.

Relationship between Chronological Age and Bone Age

Bone age is useful in monitoring the growth in children on treatment for conditions like hypothyroidism, congenital adrenal hyperplasia and growth hormone deficiency. At the same time, comparison of bone age with chronological age is useful in diagnosing various physiological and pathological causes of disorders of growth (Table 4.6). Skeletal age is more advanced in girls when compared with boys. Ideally, chronological age should be equal to bone age. These are also equal in familial short stature.

GROWTH VELOCITY

It is the rate at which the child grows over a period of time. This is calculated by measuring the height or weight gain over a period of time (Tables 4.7 and 4.8). Rather than the assessment of growth at a particular point of time, the assessment of the rate of growth over a period of time gives a more accurate clue to any deviation from normal. For example, the height is short in constitutional short stature. However, final height achieved is normal. Hence, measuring the height alone at a particular point of time will lead to a false interpretation. Height should be plotted on a growth chart so as to determine the height velocity. Height velocity <4 cm/year from 2 to 12 years of age indicates the presence of a pathological cause for short stature.

TABLE 4.6 Interpretation of the Relationship between Chronological Age (CA) and Bone Age (BA)

Relation between CA and BA	Normal	Abnormal
CA > BA (delayed bone age)	Constitutional delay Constitutional dwarfism	Chronic systemic diseases Endocrine-related hypopituitarism Hypothyroidism Male hypogonadism Malnutrition
CA < BA (advanced bone age)	Obesity	Precocious puberty Congenital adrenal hyperplasia Hyperthyroidism Chondrodystrophy

TABLE 4.7 Growth Velocity for Height in Children

Age	Growth Velocity	
	Normal	Abnormal
0–6 months	16 cm in first 6 months	< 15 cm in first 6 months
6–12 months	9 cm in next 6 months	< 7 cm in next 6 months
1–2 years	12 cm/year	< 10 cm/year
2–5 years	6 cm/year	< 5 cm/year
5–10 years	5–6 cm/year	< 4 cm/year

Note that the height gain is 25 cm in the first year. In the second year, it is half of this value. In the third year, it is one-fourth of this value.

TABLE 4.8 Growth Velocity for Weight in Children

Age	Growth Velocity
First year	6 kg
2–6 years	2 kg/year
6 years to puberty	3 kg/year

PREDICTION OF ADULT HEIGHT

The projected adult height can be calculated from the parent's height by using the following formulae for mid-parental height (MPH).

$$\text{MPH (cm) for boys} = \frac{\text{Father's height (cm)} + \text{Mother's height (cm)} + 13}{2}.$$

$$\text{MPH (cm) for girls} = \frac{\text{Mother's height (cm)} + \text{Father's height (cm)} - 13}{2}.$$

This value is plotted on the reference growth chart of height for age 18–20 years (adult equivalent). This gives an estimate of the target height for the child and the percentile that the child is likely to follow. The projected adult height is MPH ± 8.5 cm.

GROWTH MONITORING

It is important to monitor the growth of children. The first few years of life are crucial for growth and development. Periodic monitoring helps pick out the problems at an early stage. Many of the problems which affect children can be treated by early intervention.

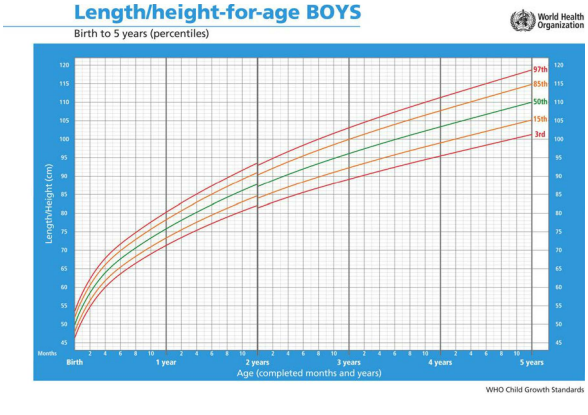
Growth Charts

These are charts which are used to assess growth by plotting changes in weight, height, etc. over a period of time (Fig. 4.2). These contain a series of curves; each of which denotes specific percentile. Percentile curves illustrate frequency distribution of children based on selected body measurements. Separate charts are used for boys and girls. National Center for Health Statistics (NCHS) growth charts are used for children till 3 years of life. A standard chart contains weight for age, height for age and weight for height. Head circumference can be marked till 3 years. The values of measurement (weight, head circumference, etc.) are given on the *y*-axis, while age of the child is given on the *x*-axis. The measurements are marked on the chart as dots. For routine monitoring, the height and weight are recorded periodically (Table 4.9). The information in each child's chart will give a percentile ranking of where the child's growth statistics falls within the population. A flat curve or a downgoing curve denotes deviation from normal pattern of growth. Early identification will help to diagnose the cause and treat at an early stage.

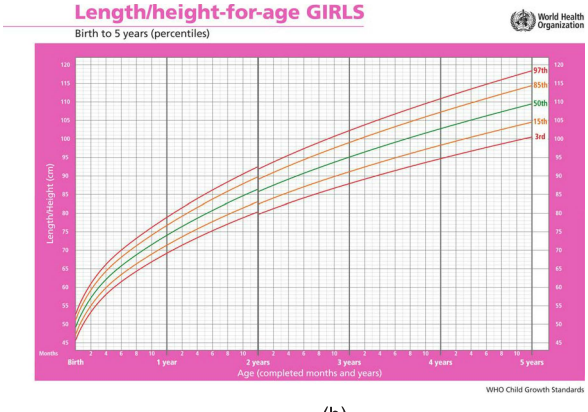
TABLE 4.9 Recommendations for Growth Monitoring

Age	Parameters	Interval
Birth to 1.5 years	Height, weight and head circumference	At birth, 6, 10, 14 weeks, 6 months, 9 months and 15–18 months
1.5–3 years	Height, weight and head circumference	6-monthly
4–8 years	Height and weight	6-monthly
9–18 years	Height, weight, BMI and sleeping metabolic rate (SMR)	Yearly

BMI, penile length and SMR should be assessed yearly from 6 years of age.



(a)



(b)

FIGURE 4.2 (a) Length/height for age (boys): birth to 5 years. (b) Length/height for age (girls): birth to 5 years.
Source: WHO (available at http://www.who.int/childgrowth/standards/en/).

ANTHROPOMETRY

Anthropometry is the study of the measurements of the human body. This gives an early clue to nutritional disorders. In acute malnutrition, there is weight loss only. In chronic malnutrition, both weight and height are less than expected for age. Anthropometry may be related to the age of the child or independent of it.

AGE-DEPENDENT AND AGE-INDEPENDENT FACTORS

Depending upon whether or not the anthropometric measurements vary with age, they can be classified as age-dependent and age-independent factors (Box 4.1). Age-dependent factors vary with the age of the child. Age-independent criteria do not vary with age and remain constant irrespective of the age.

BOX 4.1 Age-Dependent and Age-Independent Factors

Age-Dependent Factors	Age-Independent Factors
Weight	Midarm circumference (1–5 years)
Height or length	Weight for height
Head circumference	Mid-upper arm/height ratio
Chest circumference	Skinfold thickness (1–6 years)
	Enderberg index
	Kanawati index—midarm/head circumference ratio
	Rao and Singh's criteria
	Dugdale's index
	Ponderal index
	Quetelet's index
	Body mass index
	Chest/head circumference ratio

Weight

Weight is an important parameter in assessing the well-being and nutritional status of the child. Monitoring the weight is helpful in diagnosing malnutrition at an early stage. It can be monitored even by less skilled people.

1. Calculate the expected weight between the ages of 3 months and 12 years by using the following formulae (Weech's formula):
   - 3–12 months

     $$\text{Expected weight (kg)} = \frac{\text{Age (months)} + 9}{2}$$

   - 1–6 years

     $$\text{Expected weight (kg)} = \text{Age (years)} \times 2 + 8.$$

   - 7–12 years

     $$\text{Expected weight (kg)} = \frac{\text{Age (years)} \times 7 - 5}{2}$$

2. A simple formula to calculate weight in children between the ages of 2 and 12 years is

   $$\text{Weight (kg)} = \frac{[\text{Age (years)} + 3] \times 5}{2}.$$

3. From 7 to 12 years of age, weight can be calculated as

   $$\text{Age (years)} \times 3.$$

4. The expected normal increase in the weight of the children can be evaluated as follows:
   - The birth weight of a normal newborn is about 3 kg. The baby loses weight for the first 7 days and then starts gaining it, so that the weight on the 10th day is the same as the birth weight. Thereafter, the baby gains weight at a rate of approximately 30 g/day for the first 3 months. For the next 3 months, the gain in weight is approximately 20 g/day. Approximate normal gain in weight between 0 and 12 years of age is depicted in Table 4.10.
   - The baby usually doubles its birth weight by 5 months, triples by 1 year and quadruples by 2 years of age. Suppose weight of the baby at birth = X. Then the weights at various ages

are depicted as follows:

Age	Weight
At birth	*X*
5 months	2*X*
1 year	3*X*
2 years	4*X*
3 years	5*X*
5 years	6*X*
7 years	7*X*
10 years	10*X*

TABLE 4.10 Approximate Gain in Weight between 0 and 12 Years of Age

Age	Weight Gain
10 days–3 months	30 g/day
3–6 months	20 g/day
6–9 months	15 g/day
9–12 months	12 g/day
1–3 years	3 kg/year
4–12 years	2 kg/year
>12 years	5–6 kg/year (0.5 kg/month)

Height or Length

Consider length, if the child is less than 2 years of age or bedridden. The length in a newborn and infant is measured using an infantometer. Consider height if the child is more than 2 years of age. The height can be measured using a stadiometer (Fig. 4.3).

Steps to be followed before measuring the height are as follows:

- Children should stand straight with the shoes and socks removed.
- They should look straight.
- They should stand in a relaxed state with arms kept at the sides.
- They should stand with both feet and knees close together.
- The head should be kept in Frankfurt plane—the line joining the lower margin of the orbit and the upper margin of the external auditory canal should be straight.

The difference in the height and length can be up to 2 cm. The height is less than the length as the ligaments are compressed in standing posture.

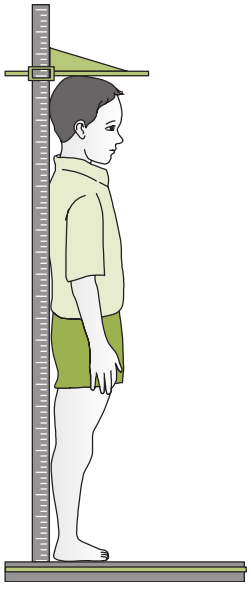


FIGURE 4.3 Measurement of height by stadiometer.

Crown-rump length can also be measured.

The length of the term newborn at birth is approximately 50 cm. At 1 year, the length is 75 cm. At 2 years, the height will be 86–87 cm. From 2 to 12 years, the height increases at the rate of 6 cm per year. At 3 years, the expected height is 93 cm. Approximate normal gain in height or length from 0 to 12 years of age is depicted in Table 4.11.

The following formula (Weech's formula) can be used to calculate the expected height from 2 to 12 years:

Expected height (cm) = (Age in years × 6) + 77.

Head Circumference

The head circumference increases due to the growth of the brain inside the skull. The rate of brain growth is rapid during the first year of life. Hence, the rate of increase in the head circumference is more in the first year of life.

The head circumference is measured by placing the tape over the occipital protuberance at the back and just over the supraorbital ridge and the glabella in front (Fig. 4.4). The expected head circumference, as the age advances, is given in Table 4.12.

Growth velocity of the head circumference is the increase in head circumference in relation

TABLE 4.11 Approximate Gain in Stature between 0 and 12 Years of Age

Age	Approximate Rate of Increase in Stature
Birth to 3 months	3.5 cm/month
3–6 months	2.0 cm/month
6–9 months	1.5 cm/month
9–12 months	1.3 cm/month
2–5 years	6–8 cm/year
5–12 years	5 cm/year

TABLE 4.12 Expected Head Circumference in Children

Age	Head Circumference (cm)
At birth	34–35
2 months	38
3 months	40
4 months	41
6 months	42–43
1 year	45–46
2 years	47–48
5 years	50–51

TABLE 4.13 Approximate Gain in Head Circumference between 0 and 5 Years

Age	Growth Velocity of the Head Circumference
0–3 months	2 cm/month
3–6 months	1 cm/month
7–12 months	0.5 cm/month
1–3 years	1 cm/6 months
3–5 years	1 cm/year



FIGURE 4.4 Measurement of head circumference.

to unit time or period (Table 4.13). Adult head circumference is usually achieved by the age of 5–6 years. The following formula (Dine's formula) is used for estimating the head circumference in the first year of life:

$$\frac{(\text{Length in cm} + 9.5) \pm 2.59}{2}.$$

Chest Circumference

It is usually measured at the level of nipples in mid-inspiration. It can also be measured at the level of xiphisternum as the position of nipples varies. It should be done in lying down position in children below 5 years of age. After this age, the measurement can be taken with the child standing. At birth, the head circumference is about 3 cm more than the chest circumference. By first year of life, both will be equal. Thereafter, the chest circumference exceeds the head circumference. This is because the rate of growth of the chest is more.

Upper Segment/Lower Segment Ratio

The length between the vertex and the pubic symphysis is the upper segment. The length between the pubic symphysis and the heel is the lower segment. To measure the upper segment, measure the height or length first. Now measure the length between the pubic symphysis and the heel. Now, calculate the upper segment by subtracting the lower segment from the height. The normal upper and lower segment ratios are given in Table 4.14.

TABLE 4.14 Normal Upper Segment/Lower Segment Ratios in Children

Age	Upper Segment/Lower Segment Ratio
At birth	1.7:1
6 months	1.6:1
1 year	1.5:1
2 years	1.4:1
3 years	1.3:1
4 years	1.2:1
7 years	1.1:1
10 years	1:1
18 years	0.9:1

This ratio is decreased in rickets due to vitamin D deficiency.

Arm Span

It is the distance between the tips of the middle fingers of both the arms when they are outstretched at right angles to the body. It is measured across the back of the child. The arm span is 1–2 cm less than the length/height in children below 5 years of age. By 10–12 years of age, both will be equal. Thereafter, arm span exceeds the height, but the difference is always less than 3 cm.

Arm span is more than height in the following conditions:

- Marfan's syndrome
- Klinefelter's syndrome
- Homocystinuria

Arm span is less than height in the following conditions:

- Achondroplasia
- Cretinism

Midarm Circumference

Midarm circumference (MAC) is 9–11 cm at birth. It grows to 16 cm by the end of first year of life. It is relatively constant between 1 and 5 years of age. It is measured with a measuring tape, midway between the acromion and olecranon process with the arm hanging by the side of the body (Fig. 4.5). The normal MAC is around 16–17 cm between 1 and 5 years.



FIGURE 4.5 Measurement of MAC..

DISORDERS OF GROWTH

Any deviation from the normal rate of growth results in disorders of growth.

SHORT STATURE

The child is said to be short-statured when the height or length is

- below 3rd percentile for age or
- more than 2 standard deviations below the mean for age.

The height velocity is usually less than 25th percentile for age.

The child is graded on the basis of McLaren's classification as follows:

I. Normal: 93%–110%
II. Short stature: 80%–93%
III. Dwarf: <80%

Evaluation of a child with short stature is done on the basis of history, examination and investigations, as discussed next.

History Taking

Name

Name gives clues to the place from where the child comes from. For example, the name *Chao-Cheng* would suggest that the child is from Japan and would be short-statured.

Age

The expected height is calculated from the age. Hence, the correct age of the child should be known, otherwise the short stature may be missed or diagnosed wrongly.

Gender

Constitutional delay in growth is more common among boys. Noonan's syndrome is seen in males. Turner's syndrome is seen in females. Growth spurt occurs earlier in females.

Place

Children from Japan are generally shorter.

Presenting Complaints

- Not gaining height
- Short for age

History of Present Illness

A detailed history should be taken to find the aetiology of short stature. The following points are relevant in a case of short stature:

- Failure to gain height
- Features of malnutrition—mental apathy, irritability, loss of weight
- Features of malabsorption—diarrhoea, steatorrhoea
- Features of cardiovascular disorders—dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea (PND), recurrent respiratory infections, cyanosis
- Features of respiratory disorders—cough, foul smelling sputum (suppurative lung disorders)
- Features of renal involvement (chronic renal failure)—polyuria, oliguria, polydipsia
- Features of hypothyroidism—intolerance to cold, constipation, hoarseness of voice, decreased activity
- Features of Cushing's syndrome—moon face, obesity, headache, vomiting, diplopia
- Features of craniopharyngioma which presses on hypothalamus and result in short stature
- Loss of weight and appetite—chronic infections (HIV, tuberculosis)
- H/o decreased activities (chronic infections)
- H/o failure to develop secondary sexual characters—menarche, axillary and pubic hair, thelarche, change in voice for boys

History of Past Illness

- H/o infections—recurrent respiratory infections (coronary heart disease, immunodeficiency, chronic respiratory conditions)
- H/o trauma—injury to growth plate in the bones
- H/o oliguria, vomiting—chronic renal failure
- H/o dyspnoea on exertion, PND, cyanosis (cardiac illness)
- H/o jaundice and bleeding (liver cell failure)
- H/o bone pain—malignancies (leukaemia, lymphoma)
- H/o difficulty in breathing, wheezing (lung disorders)

Treatment History

- H/o hospitalisation if any and its details
- H/o drugs—androgens (initially the growth is rapid but the final height achieved will be below the expected for normal age), steroids (prolonged intake results in short stature), antimalignant drugs (affect the growth)
- H/o surgery (bone surgery injuring the growth plate results in short stature)
- H/o irradiation

H/o Contact with Communicable Diseases

- H/o contact with a known case of tuberculosis—chronic tuberculous infection will be associated with short stature.

Antenatal History

- Maternal illness (cardiac disease like tetralogy of Fallot [TOF] will result in IUGR)
- Maternal infections—urinary tract infections, TORCH
- Maternal addiction—smoking, alcohol (foetal alcohol syndrome)
- Exposure to radiation
- H/o eclampsia—placental insufficiency
- H/o drug intake—phenytoin (foetal hydantoin syndrome)
- Multiple pregnancies

Birth History

- Birth weight
- Length at birth
- Term/preterm—preterm/IUGR are more prone for short stature
- Congenital anomalies
- H/o hypoxia (severe birth asphyxia results in growth retardation)

Growth and Development History

- H/o developmental delay (hypothyroidism)
- H/o decreased growth velocity (growth hormone deficiency)
- H/o precocious puberty

Nutritional History

Detailed dietary history should be taken. Chronic malnutrition is associated with short stature.

Personal History

- Food fads
- H/o behavioural disorders (anorexia nervosa)

Family History

History of short stature in other family members—information about genetic potential for the height should be obtained by recording heights of parents, siblings and other relatives. As the aetiology of short stature depends upon the inheritance and many other factors, a history of short stature even in distant relatives is important.

Social and Environmental History

- Low socioeconomic class—prone for malnutrition
- Poor hygiene (recurrent infections)
- Emotional deprivation occurs due to inappropriate psychosocial environment and lack of security. This leads to growth retardation (dwarfism)

General Examination

The child should be observed from the time he/she enters the room for general appearance and behaviour. A child with Down's syndrome is usually cheerful, friendly and hypotonic. A child suffering from hypothyroidism appears lethargic. A child with spastic gait may have short stature as a result of intracranial tumours. Such child's nutritional status may give a clue to malnutrition. Head-to-toe examination in a case of short stature is summarised in Table 4.15.

Vital Signs

- Heart rate—decreased in hypothyroidism
- Pulse—sleeping pulse rate slow in hypothyroidism, radiofemoral delay in coarctation of aorta associated with Turner's syndrome
- Respiratory rate—increased in cardiac failure, respiratory disorders like cystic fibrosis
- Blood pressure—low in cardiac failure, hypothyroidism; increased in chronic renal failure, Cushing's disease, congenital adrenal hyperplasia, neurofibromatosis type I, turner's syndrome with coarctation of aorta
- Temperature—low in hypothyroidism

Anthropometry

Determine the genetic potential of the child by measuring the mid-parental height. Other anthropometric measurements to be taken of are as follows:

- Weight—increased (hypothyroidism, Prader–Will syndrome) or decreased (chronic malnutrition, marasmus)
- Height (or length)—decreased for age
- Midarm circumference—decreased in muscle wasting due to malnutrition.
- Arm span
- Upper segment/lower segment ratio

Assess the growth velocity. If the growth velocity is less than 4 cm/year, growth hormone deficiency should be suspected.

Systemic Examination

1. Cardiovascular system—congenital cardiac disorders
2. Respiratory system—chronic lung disease
3. Central nervous system
   - Intelligence—mentally retarded children; children with cerebral palsy may have growth retardation due to poor intake
   - Visual field defects (craniopharyngioma)
   - Papilloedema—in space occupying lesions
4. Abdomen
   - Striae–Cushing's syndrome
   - Hepatosplenomegaly in congenital rubella syndrome, storage disorders, thalassaemia
   - Enlarged kidneys in polycystic kidneys
   - Ascites in hepatic failure, renal causes, nutritional causes
   - Bruits in renal artery stenosis
   - Features of liver failure (jaundice, gynaecomastia, spider naevi, palmar erythema, loss of pubic hair, flapping tremors)

TABLE 4.15 Head-to-Toe Examination in a Case of Short Stature

Examination	Clinical Features and Associated Conditions
Hair	Sparse, easily pluckable (kwashiorkor) Coarse and dry (hypothyroidism) Hirsutism (precocity, Cushing's syndrome)
Head	Microcephaly (hypothyroidism, Down's syndrome, intrauterine infections) Macrocephaly (intracranial tumours, toxoplasmosis) Large head with saddle nose (achondroplasia) Seckel's dwarfism (bird-headed dwarfism) Triangular head (Russell–Silver syndrome) Frontal bossing (rickets and thalassaemia) Craniotabes (rickets) Large fontanel (rickets, hypothyroidism, Russell–Silver syndrome)
Neck	Short neck (Down's syndrome, Klippel–Feil syndrome) Goiter (hypothyroidism) Pterygium colli/webbed neck, low posterior hairline in Turner's syndrome and Noonan's syndrome
Facies	Dysmorphic facies (Down's syndrome) Dull facies (cretinism) Doll-like facies (growth hormone deficiency) Moon facies (Cushing's syndrome)
Eyes	Brushfield spots (Down's syndrome) Visual field defects (intracranial tumour) Epicanthic folds (Down's syndrome, William's syndrome, Turner's syndrome, Noonan's syndrome) Cataract (rubella syndrome) Icterus (liver disorders) Fundus—chorioretinitis (toxoplasmosis, CMV infection)
Nose	Midfacial hypoplasia (foetal alcohol syndrome) Depressed nasal bridge (Down's syndrome) Nasal polyp (cystic fibrosis)
Oral cavity	Protruding tongue (cretinism) Glossitis (nutritional deficiency) Cleft palate, cleft lip, single central incisor (foetal alcohol syndrome) Halitosis (chronic suppurative lung disorders such as bronchiectasis and lung abscess)
Ears	Low set (Down's syndrome, Turner's syndrome, Seckel's syndrome)
Nutritional status	Malnourished (marasmus)
Skeletal abnormalities	Achondroplasia Scoliosis (Noonan's syndrome, Klippel–Feil syndrome) Pectus excavatum (Noonan's syndrome, rickets) Kyphosis

(Table continued)

TABLE 4.15 *(Continued)*

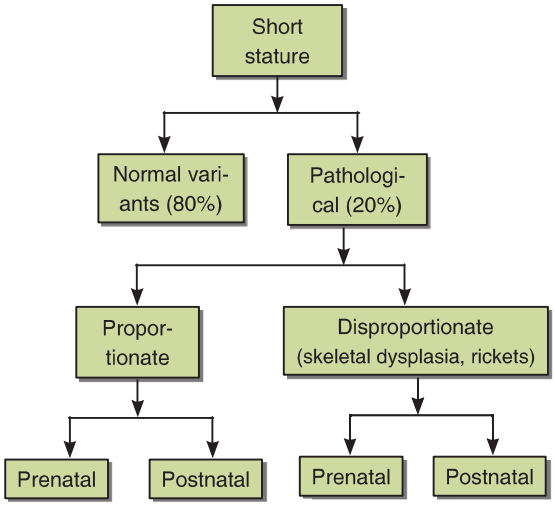
Examination	Clinical Features and Associated Conditions
Colour	Cyanosis (cyanotic heart disease) Pallor (anaemia, thalassaemia, malnutrition) Jaundice (liver disorders) Dyspigmentation (thalassaemia)
Chest	Tanner staging in girls Shield-like chest, wide-spaced nipples (Turner's syndrome) Sternal deformity (Noonan's syndrome) Costochondral beading (chondrodysplasia, rachitic rosary) Harrison sulcus (rickets)
Upper limbs	Short limbs, trident hand (achondroplasia) Short fourth metacarpal (pseudohypoparathyroidism, foetal alcohol syndrome, Turner's syndrome)
	Short fingers (Down's syndrome) Polydactyly Clinodactyly (Down's syndrome, Russell–Silver syndrome, Seckel's syndrome) Wrist widening (rickets)
Nails	Clubbing (chronic suppurative disorders, cyanotic heart disease) White nails (liver failure) Mee's lines—single transverse white line in chronic renal failure Hypoplastic nails (foetal alcohol syndrome) Hyperconvex nails (Turner's syndrome)
Palms	Palmar erythema (liver failure) Dupuytren's contracture (liver failure) Abnormal dermatoglyphics—simian crease (Down's syndrome), arch pattern in all digits (Turner's syndrome), whorl pattern (congenital rubella)
Abdomen	Protuberant (Down's syndrome) Umbilical hernia (hypothyroidism) Hepatosplenomegaly (mucopolysaccharidosis)
Lower limbs	Genu varum, genu valgum (rickets)
Skin	Skin changes of kwashiorkor Signs of nutritional deficiency Café au lait spots (neurofibromatosis type I, Fanconi's anaemia)
Genitalia	Testis—cryptorchidism, micropenis (hypopituitarism) Hypospadias, cryptorchidism (Noonan's syndrome) Testicular volume estimation

5. Genitalia and secondary sexual characters
   - Precocious puberty (congenital adrenal hyperplasia)
   - Secondary sexual characters—delayed in nutritional disorders, chronic systemic disorders, endocrine disorders (hypopituitarism)

Investigations

1. X-ray (skeletal survey)
   - Bone age
   - X-ray of skull in a case of pituitary tumour shows enlargement of sella turcica
   - Suprasellar calcification (craniopharyngioma)
2. Blood and urine tests
   - Complete blood count—infections
   - Erythrocyte sedimentation rate (ESR)—chronic inflammatory and collagen vascular disorders
   - Blood sugar, renal function tests, serum calcium, phosphorus
   - Liver—SGOT, SGPT, serum albumin
   - Serum total protein, albumin/globulin ratio (malnutrition)
   - Serum calcium, phosphorus, alkaline phosphatase (rickets)
   - Blood sugar—fasting/postprandial (diabetes)
   - Urine pH, blood urea, creatinine renal function tests (renal tubular acidosis)
   - Thyroid function tests—serum T4, thyroid-stimulating hormone (TSH) (hypothyroidism)
3. Stools—giardiasis
4. Karyotyping
5. Tests for growth hormones
   - 24-hour growth hormone level
   - Growth hormone level (after induction by hypoglycaemia)
6. Cortisol production (after induction by hypoglycaemia)
7. Renal function tests
8. Tests for malabsorption

Classification



Normal Variants (80%)

- Familial
- Racial
- Constitutional

Pathological Short Stature

1. Prenatal causes
   - Primordial dwarf
   - IUGR
   - Placental disease
   - Intrauterine infections—TORCH
   - Teratogens
   - Genetic disorders—achondroplasia
   - Progeria (premature ageing)
   - Chromosomal disorders—Down's syndrome, Turner's syndrome, Noonan's syndrome, William's syndrome, Cri-du-chat syndrome, Silver–Russell syndrome, Prader–Willi syndrome, Seckel's dwarf, Bloom syndrome
2. Postnatal causes
   - Malnutrition
   - Chronic systemic disorders—congenital heart diseases, asthma, cystic fibrosis, chronic renal failure, renal tubular acidosis,

chronic anaemia, chronic infections (tuberculosis), chronic diarrhoea, malabsorption syndromes, celiac disease, inflammatory bowel disease
- Endocrine disorders—hypopituitarism, hypothyroidism, Cushing's disease, hypogonadism, adrenal hypoplasia, GH insensitivity
- Skeletal disorders—rickets, achondroplasia, osteogenesis imperfecta, chondrodystrophy, osteopetrosis, vertebral column infection, tuberculosis (Pott's spine), spinal cord injury
- Metabolic disorders—mucopolysaccharidosis, Wilson's disease, glycogen storage disorders
- Drugs—steroids
- Psychosocial short stature—eating disorders, emotional deprivation
- Idiopathic

Proportionate Short Stature. The upper segment to lower segment ratio is normal for age (Table 4.14). The causes of proportionate short stature are as follows:

- Familial
- Constitutional
- IUGR
- Nutritional deficiency
- Chronic visceral disorders
- Endocrine disorders—growth hormone deficiency, Cushing's syndrome
- Psychosocial deprivation
- Miscellaneous—McCune–Albright syndrome, Laurence–Moon–Biedl syndrome, Sotos' syndrome, Frohlich's syndrome

Disproportionate Short Stature. The upper segment to lower segment ratio is not normal for age. It can be of the following types:

1. Short limbs. These children have infantile proportions and are further classified as given in Table 4.16. It occurs in the following conditions:
   - Achondroplasia
   - Hypochondroplasia
   - Chondrodysplasia
   - Diastrophic dysplasia
   - Rickets
   - Osteogenesis imperfecta (Fig. 4.6)
   - Cretinism (Fig. 4.7)
2. Short trunk
   - Mucopolysaccharidosis—Morquio's disease (Fig. 4.8)



FIGURE 4.6 Dwarfism in a child with osteogenesis imperfecta. The child has multiple skeletal deformities due to fractures.



FIGURE 4.7 Short stature in a child with hypothyroidism.



FIGURE 4.8 Short stature in a child with mucopolysaccharidosis. The child also has coarse facies and mental retardation.

TABLE 4.16 Classification and Causes of Short Limbs

Classification	Part Shortened	Causes
Rhizomelic	Proximal	Achondroplasia, hypochondroplasia
Mesomelic	Middle	Langer mesomelic dysplasia
Acromelic	Distal	Acromelic dysplasia

- Mucolipidoses
- Caries spine
- Hemivertebra
- Spondyloepiphyseal dysplasia
- Spondyloepimetaphyseal dysplasia
- Metatropic dwarfism
- Kniest syndrome

Salient Features of Some Causes of Short Stature

Familial/Genetic Short Stature

- Parents, either or both, are short statured.
- Length is normal or small at birth.
- Rate of increase in height is normal.
- Child fails to achieve the normal adult height but the predicted adult height is appropriate to the familial pattern.
- Bone age is equal to chronological age.
- Adequate balanced nutrition may improve the height. The height achieved by the child depends on the parent's height. When both the parents are short, the ultimate height achieved by the child will be short.
- The sexual maturation is normal.
- Treatment—reassurance.

Constitutional Short Stature

- History of delayed puberty and delayed height spurt in one or both parents.
- Birth weight and length are normal.
- Rate of growth is normal initially for 4–12 months but decelerates later.
- Bone age is slightly less than chronological age and corresponds to the height age (bone age = height age).
- Ratio between upper segment and lower segment is normal or slightly immature.
- Human growth hormone and gonadotropin levels are normal. Sexual maturation and pubertal growth spurt are delayed.
- Final height achieved is normal.
- Common in boys than in girls.
- Absence of rise of GH in the pubertal period.
- Treatment—no drugs are usually needed as this is not a disorder but variation in normal growth. In few cases, testosterone enanthate 50–100 mg every 2–3 weeks can be given for 4–6 months to accelerate the linear growth and unusual delay in onset of puberty.

Growth Hormone Deficiency

Growth hormone is needed for the normal growth of the child. In its deficiency, the rate of growth of the child is regular but slow after birth. The child is normal at birth. Growth velocity is decreased. The growth hormone deficiency can be partial or total, isolated or associated with panhypopituitarism (usually after removal of craniopharyngioma). Failure to respond to growth hormone indicates end-organ growth hormone receptor defects (Laron's syndrome). This should be differentiated from primary growth hormone deficiency.

Features

- Proportionate short stature
- Reduced growth velocity (<4 cm/year) for age and pubertal stage
- Increased amount of fat around the waist
- Immature facial appearance
- Normal intelligence
- Delayed dental development
- Delayed onset of puberty
- Bone age less than chronological age

Investigations

- Insulin-like growth factor 1 (IGF-1) and IGF-binding protein 3 (IGFBP-3)—low values suggest growth hormone deficiency but are not diagnostic.
- Growth hormone assay—circulating levels of growth hormone are decreased in growth hormone deficiency and increased in Laron's syndrome.
- Growth hormone stimulation tests—peak growth hormone levels less than 10 ng/mL 20–30 minutes after provocative stimuli suggest growth hormone deficiency. Provocative stimuli include exercise, insulin-induced hypoglycaemia, arginine, levodopa, clonidine and glucagon.
- Testing functions of the pituitary–hypothalamus axis—injection of TRH causes an increase in the level of the TSH and prolactin if the pituitary gland is normal. If the lesion is in the pituitary gland, then there is no increase in these levels.
- CT/MRI scan of the brain—to rule out craniopharyngioma or other CNS lesions.

Treatment

- In children with growth hormone deficiency, treatment with growth hormone should be started as early as possible.
- Recombinant growth hormone is given in a dose of 0.18–0.3 mg/kg/week subcutaneously in children. Higher doses are needed during puberty.
- Growth hormone is also given in other conditions such as Turner's syndrome, chronic renal failure, idiopathic short stature, small-for-gestational-age (SGA) infants who do not show catch-up growth by 2 years of age and Prader–Willi syndrome. Higher doses are required in these conditions and the results are variable.
- Regular monitoring for height and bone age is done to determine the time of discontinuation of therapy. Criteria to stop growth hormone treatment include growth rate <1 inch in 1 year, bone age >14 years in girls and >16 years in boys. Adverse effects of growth hormone include pseudotumour cerebri, hyperglycaemia, slipped capital femoral epiphysis, hypothyroidism and adrenal insufficiency.
- Luteinising-hormone-releasing hormone can be given along with growth hormone. This will delay the epiphyseal fusion and will prolong the skeletal growth.
- Recombinant IGF-1 can also be given subcutaneously, twice daily.

Hypothyroidism

Hypothyroidism refers to deficiency of thyroid hormones in the body (see Chapter 14).

Clinical Features. The deficiency of thyroid hormone leads to cretinism. The features of cretinism are as follows:

- Short stature, immature upper segment/lower segment ratio
- Delayed closure of fontanels
- Mental retardation
- Dull facial expression, puffy and cretinoid
- Macroglossia (protruding tongue)
- Constipation
- Markedly delayed bone age
- Infantile sexual development
- Delayed puberty

Investigations

- Plasma TSH, T_3 and T_4 levels are estimated.
- Blood cholesterol may be increased.

Treatment

- Thyroid hormone replacement

Differences between cretin and pituitary dwarf are given in Table 4.17. Differences between short stature due to Down's syndrome and cretinism are given in Table 4.18.

Turner's Syndrome

The most common karyotype is 45,X. The child usually presents with short stature, delayed puberty and

TABLE 4.17 Differences between Cretin and Pituitary Dwarf

Features	Cretin	Pituitary Dwarf
Aetiology	Decreased thyroxine levels	Decreased pituitary functions
Appearance	Coarse facies	Doll-like facies
Intelligence	Decreased	Normal
Genital development	Normal	Sexual infantilism
Treatment	Thyroxine	Growth hormone

classical features (for features of Turner's syndrome see Chapter 15). Differentiating features of various types of short stature are given in Table 4.19.

Primordial Dwarfism

Primordial dwarfism is a very rare form of dwarfism in which the body is properly and proportionately formed, but remains quite tiny. All the bones and organs of the body are proportionally smaller than in an average person. The exact definition can vary from one type to another, but all are defined primarily by extreme short stature at birth. The lack of normal growth in the disorder is not due to a deficiency of growth hormones, as in hypopituitary dwarfism. Some of the subtypes of primordial dwarfism are Majewski osteodysplastic primordial dwarfism ([MOPD] types I, II and III), Seckel syndrome, Russell–Silver syndrome and Meyer–Gorlin syndrome.

TABLE 4.18 Differences between Down's Syndrome and Cretinism

Features	Down's Syndrome	Cretinism
Aetiology	Chromosomal disorder	Endocrine abnormality resulting in thyroxine deficiency
Appearance	Cheerful, active	Dull, repulsive, lethargic
Head	Microcephaly with flattening of occiput	Microcephaly
Skin	Fine, tender	Thick, rough
Eyes	Upward slant Epicanthic fold	Normal slant No epicanthic fold
Tongue	Protruding, furrowed Normal size	Large protruding tongue
Dermatoglyphics	Simian crease	Normal
Congenital defects	High incidence of Hirschsprung's disease, duodenal atresia	No predisposition to congenital defects
Investigations	Karyotyping	Low thyroxine levels
Complications	Leukaemia	Myopathy
Treatment	No definitive treatment	Replacement
Prognosis	Maximum IQ obtained is of an 8-year-old child	With adequate replacement therapy in the first few months of life, IQ of the child will be normal

TABLE 4.19 Differentiating Features of Various Types of Short Stature

Features	Constitutional	Familial	Hypopituitarism	Hypothyroidism	Turner's Syndrome
Family history	Positive	Positive	Usually negative	Negative	Usually negative
Birth height and weight	Normal	Low	Normal	Normal	Low
Rate of growth	Slow from infancy	Normal	Slow from few months after birth	Slow from birth	Slow from birth
Epiphyseal development	Progressive retardation	Normal	Progressive retardation	Severe retardation	Variable
Puberty	Delayed	Normal	Delayed	Delayed	Delayed
Growth hormone	Normal	Normal	Low	Normal	Variable
Gonadotrophin levels	Normal	Normal	Low, except in isolated GH deficiency	Variable	High

Features

- Bone age normal/moderately delayed
- Craniofacial disproportion
- Decreased potential for growth; small at birth and remains small throughout life
- IUGR
- Sexual maturation at normal age

Treatment. There is as yet no effective treatments for primordial dwarfism.

Nutritional Dwarfism

It occurs due to nutritional deficiency. Acute malnutrition results in reduction in the weight alone. The height is normal for age in these children. If the duration of the malnutrition is long, the weight and the height are affected. A detailed assessment of these children with nutritional history, anthropometric measurements and other associated nutritional deficiency symptoms should be done.

Features

- Long-standing protein energy malnutrition
- Iron deficiency anaemia may be present
- Bone age usually slightly less than the chronological age

Treatment. A proper diet plan should be calculated and advised.

Emotional Deprivation Dwarfism

It is also known as psychosocial dwarfism. There is deficiency of growth hormone and adrenocorticotropic hormone (ACTH) due to functional hypopituitarism. It improves with adequate care, love and affection.

Chronic Systemic Disorders

The following factors may contribute to growth retardation in chronic systemic disorders:

- Decreased appetite
- Poor intestinal absorption
- Increased basal metabolic rate/catabolism
- Decreased somatomedin in chronic renal diseases and liver diseases
- Decreased growth hormone levels
- Hypothalamic suppression

Skeletal Dysplasias

These are heterogenous group of disorders which are characterised by abnormal cartilage and bone growth. These are also known as osteochondrodysplasias. Examples include cleidocranial dysostosis, chondroplasia, achondroplasia, hypochondroplasia, diastrophic dwarfism and Ellis–van Creveld syndrome (chondroectodermal dysplasia).

Features

- Disproportionate skeletal proportions
- Short stature
- Delayed motor milestones
- May be associated with mental retardation
- Family history often present

Treatment. Bone lengthening procedures can be tried.

Idiopathic Short Stature

Features

- Short stature
- Cause not known
- Parent's height normal
- Family history absent
- No known functional abnormality
- Growth velocity reduced

Treatment. Growth hormone may be useful.

Mucopolysaccharidoses

Mucopolysaccharidoses are a group of metabolic disorders caused by the absence or malfunctioning of lysosomal enzymes needed to break down molecules called glycosaminoglycans (GAGs) (long chains of sugar carbohydrates). GAGs are an important constituent of the extracellular matrix, joint fluid and connective tissue throughout the body. Progressive accumulation of GAGs within the cells of various organs ultimately compromises their function. These are inherited in an autosomal recessive manner, except Hunter's which is X-linked recessive.

Clinical Features

- Normal intellect or may be profoundly retarded, may experience developmental delay or may have severe behavioural problems

- Hearing loss—either conductive or neurogenic, or both
- Communicating hydrocephalus
- Cloudy cornea, glaucoma and degeneration of the retina
- Dysmorphic facies—coarse facial features (flat nasal bridge, thick lips and enlarged mouth and tongue)
- Short stature with disproportionately short trunk (dwarfism)
- Skeletal dysplasia
- Thickened skin
- Hepatomegaly and splenomegaly
- Hernias
- Excessive body hair growth
- Short and often claw like hands, progressive joint stiffness and carpal tunnel syndrome can restrict hand mobility and function
- Recurring respiratory infections are common, as are obstructive airway disease and obstructive sleep apnoea. Many affected individuals also have heart disease, often involving enlarged or diseased heart valves

Radiological Findings

- Bullet-shaped metacarpals
- Beaking of lower thoracic and upper lumbar vertebra
- Thickened calvarium
- Dysostosis multiplex
- Flexion deformity of fingers
- Hockey-stick–shaped sella turcica or J-shaped sella turcica
- Ulna and radius facing each other

Treatment. Currently there is no cure for these disorders. Medical care is directed at treating systemic conditions and improving the person's quality of life. Physical therapy and daily exercise may delay joint problems and improve the ability to move.

Achondroplasia

Achondroplasia is inherited as an autosomal dominant condition. It is the most common cause of short stature with disproportionately short limbs.

Clinical Features

- Dysmorphic facies—large head with frontal bossing, hypoplastic mid-face with cheekbones that lack prominence and a low nasal bridge with narrow nasal passages
- Short fingers with trident hand (divergence between ring and middle finger)
- Hyperextensibility of the joints
- At birth there is often prominence of the mid-to-lower back with a small gibbus (a hump). With walking, the hump goes away and a pronounced sway (lordosis) of the lumbar region (the lower back) becomes apparent. The lumbar lordosis is persistent. There is cord compression at foramen magnum
- Genu varum
- Hypotonia
- Normal intelligence, enlargement of brain (megalencephaly)
- Other features like deafness and delayed walking

X-ray Findings

- Short pelvis
- Broad iliac wings
- Vertebra interpaeduncular distance diminished from L1 to L5
- Posterior scalloping of vertebra
- Shortened base of skull
- Small and irregular foramen of magnum
- Narrow deep sciatic notches
- Horizontal acetabular roofs

Treatment. At present, there is no treatment for achondroplasia. However, if desired, limb-lengthening procedure may be tried in some cases.

Foetal Alcohol Syndrome

It occurs due to maternal intake of alcohol. The salient features are as follows:

- Short stature
- Characteristic facies—midfacial hypoplasia, railroad track ear, epicanthal folds, reduced palpebral fissure length/inner canthal distance ratio, low set ears, short upturned nose, hypoplasia of maxilla, micrognathia
- Microcephaly and mental retardation
- Delayed developmental milestones
- Cardiac defects—atrial septal defect, ventricular septal defect, aberrant great vessels, TOF
- Skeletal abnormalities—radioulnar synostosis, hemivertebra, Klippel–Feil syndrome, clinodactyly,

pectus excavatum, pectus carinatum, short fifth digit
- Behavioural disorders—impulsive behaviour, intellectual dysfunction, attention deficit hyperactivity disorder
- Growth retardation—intrauterine and postnatal growth retardation
- Hearing loss (conductive/neurosensory)
- Renal abnormalities—aplastic/hypoplastic kidneys, hydronephrosis, horse shoe kidneys

TALL STATURE

When the crown-heel length is more than 97th percentile for normal population of same age and sex, or more than two standard deviations above the mean for the population, it is called tall stature. The conditions causing tall stature can be genetic, metabolic or environmental. Evaluation includes history taking, clinical examination, estimation of growth potential, laboratory investigations and gene analysis.

History Taking

1. Age of the patient is important to calculate the expected height. Inaccurate age will give a wrong impression of tall stature
2. Gender
   - Males are taller than females
   - Eunuchs are taller
   - Klinefelter's syndrome is seen in males
3. Race—it is important to know the native place to which the child belongs. For instance, the children from America are taller while those from Japan are shorter
4. Presenting complaints
   - Abnormally tall for age
   - Precocious puberty
5. History of present illness
   - Headache (pituitary tumours)
   - Visual disturbances (pituitary tumours)
   - Precocious puberty
6. History of past illness—onset of puberty
7. Antenatal history—Klinefelter's syndrome is associated with advanced maternal age
8. Birth history—it is important to know the birth weight, length and head circumference of a child who presents with tall stature. Birth length is more in Beckwith–Wiedemann syndrome and Sotos' syndrome
9. Neonatal history—convulsions (due to hypoglycaemia, common in Beckwith–Wiedemann syndrome)
10. Developmental history—mental retardation is seen in Sotos' syndrome, Marfan's syndrome and homocystinuria
11. Family history—tall parents have tall children
12. Socioeconomic history—exogenous obesity is common in upper socioeconomic class

Clinical Examination

The following features should be looked for during the head-to-toe examination of any child who presents with tall stature.

1. Tall stature
2. Mental retardation (cerebral gigantism)
3. Asymmetry of the body—hemihypertrophy is seen in
   - Beckwith–Wiedemann syndrome
   - McCune–Albright syndrome
   - Neurofibromatosis type 1
4. Dysmorphic features
   - Sotos' syndrome (cerebral gigantism)
   - Beckwith–Wiedemann syndrome
   - Klinefelter's syndrome
   - Marfan's syndrome
5. Head
   - Large irregular head
   - Prominent forehead (cerebral gigantism)
6. Eyes
   - Prominent eyes (Beckwith–Widemann syndrome)
   - Hypertelorism (cerebral gigantism)
   - Antimongoloid slant of palpebral fissures (cerebral gigantism)
7. Mouth
   - High-arched palate (Marfan's syndrome, cerebral gigantism)
   - Cleft palate (Beckwith–Widemann syndrome)

- Tongue enlarged—macroglossia (Beckwith–Widemann syndrome)

8. Jaw
   - Prognathism (cerebral gigantism)
9. Ears
   - Abnormal transverse crease in the pinna of the ear (Beckwith–Widemann syndrome)
10. Hands
    - Arachnodactyly (Marfan's syndrome)
    - Spade-like hands (acromegaly)
11. Foot
    - Pes planus (Marfan's syndrome)
12. Skin
    - Facial nevus flammeus (Beckwith–Widemann syndrome)
    - Café au Lait spots (McCune–Albright syndrome)
    - Vascular nevus (Klippel–Trenaunay syndrome)
13. Abdomen
    - Exomphalos, omphalocoele (Beckwith–Widemann syndrome)
    - Visceromegaly—liver and kidneys (Beckwith–Widemann syndrome)
14. Signs of virilism
    - Enlargement of clitoris
15. Features of hyperthyroidism
    - Tremors
16. Musculoskeletal system (Table 4.20)
    - The bony deformities like scoliosis are common in children with tall stature.
    - Clumsy movements (cerebral gigantism).

TABLE 4.20 Examination Findings in Musculoskeletal System

Bony Deformities	Associated Conditions
Scoliosis—ask the patient to bend and touch the toes to determine the presence of scoliosis	Marfan's syndrome Homocystinuria Proteus syndrome Sotos' syndrome Neurofibromatosis
Kyphosis	Acromegaly Gigantism
Genu recurvatum	Marfan's syndrome
Extensibility of joints	Limited in homocystinuria Hyperextensibility of thumb to radius in Marfan's syndrome
Arachnodactyly	Marfan's syndrome
Thumb sign—thumb projects beyond the ulnar border on fisting of the hand	Marfan's syndrome
Wrist sign—wrap the fingers of one hand around the wrist. The distal phalanx of the fifth finger overlaps the distal phalanx of thumb	Marfan's syndrome

Anthropometry

- Increased height
- Increased weight in Beckwith–Widemann syndrome
- Height velocity
- Weight for height
- Head circumference—increased in cerebral gigantism (Sotos' syndrome), decreased in microcephaly (Beckwith–Widemann syndrome)
- Upper segment/lower segment ratio—lower segment is more than upper segment in Marfan's syndrome
- Body mass index
- Arm span is increased in Marfan's syndrome
- Parent's height—Mid-parental height is helpful to diagnose constitutional or familial tall stature
- Final height assessment

Estimation of Growth Potential

- Height velocity which is defined as the rate of growth over fixed time interval should be assessed. The velocity in the normal children should oscillate around 50th percentile. The height velocity is maximum from birth to 6 months of life. If the height velocity remains >97th percentile for over a year, the child should be evaluated for tall stature. If the height velocity remains between 75th and 97th percentile for over a year, the child should be observed for further 1 year.
- Child's height should be compared with the mid parental height. He should be investigated and treated accordingly.

Investigations

1. Blood glucose (decreased in Beckwith–Wiedemann syndrome)
2. Amino acid screening (homocystinuria)
3. Hormonal assays
   - Growth hormone level (increased in gigantism)
   - Thyroid screening test (increased thyroid hormones/TSH in hyperthyroidism)
   - Androgen levels (increased in precocious puberty)
   - Oestrogen level (increased in precocious puberty)
   - 17-hydroxyprogesterone (increased in CAH)
   - Insulin-like growth factor-1
4. Bone age—X-ray may show normal or advanced bone age
5. Karyotyping (chromosomal disorders)

Arriving at the Diagnosis

The following points are helpful in evaluating children with tall stature and arriving at a diagnosis:

1. Normal clinical examination findings, normal bone age, no dysmorphic features—constitutional tall stature
2. Normal clinical examination findings, no dysmorphic features, advanced bone age—obesity, growth hormone excess, precocious puberty
3. Dysmorphic features with proportionate growth—Beckwith–Widemann syndrome, Weaver–Smith syndrome
4. Dysmorphic features with disproportionate growth—Klinefelter's syndrome, Sotos' syndrome
5. Tall stature with normal height velocity—familial, constitutional
6. Tall stature with increased height velocity—idiopathic
7. Associated with precocious puberty, rapid growth rate and advanced bone age
   - Gonadotrophin-dependent precocious puberty—gonadal tumours, gonadotrophin-producing tumour
   - Gonadotrophin-independent precocious puberty—pituitary adenoma, congenital adrenal hyperplasia, XYY syndrome
8. Not associated with precocious puberty—gigantism (growth hormone excess), hyperthyroidism

Treatment

- The aim is to limit the final adult height by giving sex hormones (Table 4.21). Treatment is continued till the time of epiphyseal fusion. This is associated with long-term complications.
- Treatment of primary cause if possible. For instance, treatment of pituitary adenoma.

TABLE 4.21 Drugs Used in Precocious Puberty

Sex	Drug	Dose	Duration
Males	Testosterone	250 mg intramuscularly every week	6 months
Females	Ethinyl estradiol	0.15–0.5 mg/day orally	During first 12–14 days of the menstrual cycle

Associated Conditions

Familial Tall Stature

This is due to intrinsic cause (genetic and familial). The features are as follows:

- Most common type
- Child is tall from early childhood
- Tall parents
- High normal growth rate
- Physical examination normal
- Bone age = chronological age
- Tall stature is appropriate to family

Constitutional Tall Stature

The features of constitutional tall stature are as follows:

- Common in females
- Family history positive
- No dysmorphism
- Normal length at birth, tall stature evident by 3–4 years of age

- Accelerated growth velocity in the early childhood but slows down after 4–5 years when the growth curve parallels the normal curve
- Normal height velocity after 4–5 years of life
- Final adult height lies at the upper limit of normal
- Early induction of normal puberty
- Somatomedin-C levels fall as oestrogen levels fall
- Conjugated oestrogen can be used for treatment

Differences between familial and constitutional tall stature are given in Table 4.22.

Excess Growth Hormone

Gigantism is due to overproduction of growth hormones before the closure of epiphysis. *Acromegaly* (in adults) occurs due to overproduction after fusion of epiphysis. Growth hormone excess results in rapid linear growth. There will be insulin resistance.

Growth hormone excess is due to growth hormone secreting tumours, which are categorised as:

- Pituitary tumours—pituitary adenoma, hypothalamic tumour secreting growth-hormone-releasing hormone
- Non-pituitary tumours—lung tumours, pancreatic tumours, adrenal gland tumours

TABLE 4.22 Differences between Familial and Constitutional Tall Stature

Features	Familial or Genetic Tall Stature	Constitutional Tall Stature
Incidence	Most common type	Second most common
Mean birth length	Increased length	Normal length at birth
Growth velocity	High normal growth rate, tall from early childhood	Accelerated in early childhood but slows down after 4–5 years when the growth curve parallels the normal curve
Family history	Tall stature is appropriate to family	Similar growth pattern in the family. One or both parents may be tall
Puberty	Pubertal growth spurt at an earlier age	Develops in the early range of normal
Final height	Tall	Upper range of normal

Features

- Behaviour changes
- Fatigue—early symptom
- Macrocephaly
- Coarse facies—broad nose, tongue enlarged
- Large hand and feet
- Increased height
- Increased weight
- Increased head circumference
- Distal parts of the body are more involved in acromegaly

Investigations

- Glucose tolerance test for growth hormone secretion
- MRI head—pituitary adenoma, sella turcica enlargement
- Radioimmune assay for growth hormones—increased growth hormone levels
- Visual field defects—pituitary adenoma
- Hormonal assays—cortisol (9:00 am), prolactin, testosterone, luteinising hormone (LH), follicle-stimulating hormone (FSH)
- X-ray of heel— increased heel pad thickness
- X-ray of hand—tufting of phalanges
- Pituitary biopsy—eosinophil cells

Treatment

- Medical therapy—bromocriptine, octreotide
- Surgery—hypophysectomy
- Irradiation

Congenital Adrenal Hyperplasia

- Tall stature
- Accelerated puberty
- Accelerated bone age
- Increased dehydroepiandrostenedione (DHEA) levels

See Chapter 14 for details.

Hyperthyroidism

- Tall stature in childhood
- Growth rate—rapid
- X-ray—advanced bone age and premature fusion of bones
- Thyroid screening—T_3 and T_4 elevated, TSH decreased

- Treated with antithyroid drugs—propylthiouracil (100–150 mg three times a day) or methimazole 30 mg once daily
- Subtotal thyroidectomy or radioiodine useful in few cases

Hypogonadism

Bones continue to grow in linear manner until the epiphysis fuse. Normally epiphyseal fusion is accelerated by testosterone. In hypogonadism, testosterone levels are decreased. Hence, fusion is delayed and the growth continues.

Homocystinuria

- Inborn error of methionine metabolism
- Inheritance—autosomal recessive
- Cystathionine-β-synthase deficient in type 1 (most common)
- Gene for cystathionine-β-synthase present on long arm of chromosome 21

Marfan's Syndrome

It is caused due to impaired collagen synthesis as a result of mutation in the *FBN1* gene which encodes a connective protein called fibrillin-1, a component of extracellular matrix. *FBN1* gene is located on chromosome 15q-21.1. Inheritance is autosomal dominant. It classically involves the musculoskeletal system, eyes and cardiovascular system, but it also significantly involves the lungs, skin and CNS. Its features are as follows:

- Tall stature with long slender limbs and long fingers and toes (arachnodactyly)
- Dislocated lenses
- Aortic root dilatation
- Increased height
- Lower segment > upper segment. Ratio of upper segment to lower segment is decreased
- Arm span > height

Klinefelter's Syndrome

- One of the most common causes of primary hypogonadism
- Incidence is 1:1000 in low-birth-weight babies.
- 47,XXY or 48,XXYY
- Diagnosed usually after puberty
- Features—long lower limbs, overweight

XYY Syndrome

- Patients have one more Y chromosome due to non-disjunction (47,XYY or 48,XYYY).
- Incidence is 1 in 800 to 1 in 700 males.
- 47,XYY boys have an increased growth velocity during early childhood.
- Average final height is few centimetres above expected final height.
- Usually detected only during genetic analysis for some other reason because many have normal appearance and normal fertility.
- Behaviour is abnormal.
- Normal intelligence.
- The patients are at risk for learning disability and hyperkinetic behaviour.

Sotos' Syndrome (Cerebral Gigantism)

- Dysmorphic facies
- Abnormally tall
- Birth weight and length—large for age at birth
- Bone age—advanced
- Growth rapid during 4–5 years of age
- Puberty at normal or early age
- Growth hormone levels—normal
- CT scan will show dilatation of lateral and third ventricles

Beckwith–Wiedemann Syndrome

- Dysmorphic facies
- Tall stature
- Chromosome 11p15—partial duplication of chromosome 11p
- Birth weight—large for date

McCune–Albright Syndrome

- Dysmorphic facies
- Tall stature
- Polyostotic fibrous dysplasia
- Bone age—advanced

Klippel–Trenaunay Syndrome

It is a variant of hereditary angiodysplasia. The features are as follows:

- Gigantism
- Vascular nevus

- Hypertrophy of bone and soft tissue
- Unilateral varicosis

Proteus Syndrome

Overgrowth of various parts of the body starts in the first few years of life. The overgrowth can affect the whole body or one side of the body or a part of the body.

UNDERWEIGHT

A child whose body weight is less than that expected for age is said to be underweight. The criteria are given in Table 4.23. For management of undernutrition, see Chapter 5.

PREDISPOSING CAUSES

- Decreased intake—anorexia nervosa, malnutrition, low socioeconomic class, poverty
- Diseases—bronchitis, chronic illness, chronic diarrhoea, infections, worm infestations, cardiac failure, kidney failure, inflammatory bowel disease, malabsorption, malignancy, metabolic disorders, liver diseases
- Emotional causes—depression
- Endocrine—hyperthyroidism, diabetes mellitus type 1, Addison's disease
- Excess exercise
- Genetic factors

TABLE 4.23 Anthropometric Parameters

Parameters	Criteria for Underweight
Body weight	18% less than IBW
Weight for age	<80% of the standard weight
Body mass index (BMI)	<18.5 <5th percentile for age and sex

OBESITY

Obesity is a condition with excess amount of body fat. There is an increase in the number and size of adipocytes. A child whose weight for age is between 110% and 120% of the standard weight is known as overweight, while that more than 120% of the standard weight is obese. Criteria for obesity are as follows:

- Child has a weight for age and sex above 120% of the standard weight, or
- body weight is more than the ideal body weight (IBW) by 20%, or
- BMI is more than 95th percentile for age and sex.

HISTORY TAKING

Age

Correct age is required to calculate the expected weight. If the exact age is not known, there is a possibility of missing overweight or obesity.

Sex

The skinfold thickness varies with sex and is more in females.

Presenting Complaints

The child presents with overweight.

History of Present Illness

- Decreased activity
- Binge eating/abnormal food eating behaviour
- Lack of satiety
- H/o hyperphagia—lesions of hypothalamus, craniopharyngioma
- H/o early development of secondary sexual characters like pubic hair, change in voice, menarche, the thelarche—precocious puberty
- H/o delayed development of secondary sexual characters—hypothyroidism
- H/o decreased activities—hypothyroidism
- H/o constipation—hypothyroidism
- H/o headache, visual disturbances—pituitary tumour
- H/o psychological maladjustment with the other family members

History Related to Complications

- H/o headache—hypertension
- H/o joint pain—arthritis

- H/o depression—psychological problems
- H/o exercise intolerance—respiratory insufficiency, cardiac problems
- H/o backache
- H/o difficulty in breathing—obstructive sleep apnoea and asthma
- H/o jaundice—due to obstruction of bile duct by gall stones

History of Past Illness

- H/o head injury
- H/o meningitis/encephalitis (polyphagia is common after CNS infections)

Treatment History

- H/o intake of steroids—long-term intake of steroids predispose to Cushing's syndrome
- H/o intake of other drugs that may predispose to obesity—insulin, sulfonylurea, thiazolidinediones, atypical antipsychotics, antidepressants, hormonal contraceptives, anticonvulsants like phenytoin and valproate

Antenatal History

- H/o diabetes in the mother (infant of a diabetic mother will be large)

Postnatal History

- Big baby may be associated with difficulty in delivery or delivery by caesarean section
- Birth weight (more weight is associated with high risk for obesity in later life)

Dietary History

- Diet intake—increased intake of calories
- Junk foods
- Feeding habits—frequent feeding, snacks in between meals, overeating

Personal History

- Play activities less
- Sedentary habits (television watching)
- Psychosocial problems
- Behaviour pattern of the child

Family History

If other members of the family are obese, there are more chances that the child is obese.

Socioeconomic History

- Working mother
- Upper socioeconomic class

GENERAL EXAMINATION

- Obese (Fig. 4.9)
- Mental retardation—hypothyroidism
- Facial dysmorphism—Laurence–Moon–Biedl syndrome
- Evidence of endocrine dysfunction such as precocious puberty
- Secondary sexual characters

Anthropometry

- Height—less in hypothyroidism, more in overnutrition
- Weight—more than 120% of the expected
- Skinfold thickness—increased
- Weight for height—increased
- BMI—increased

AETIOLOGY

Aetiology is multifactorial. A number of conditions predispose to overweight and obesity. Some of these are as follows:

A	Activity—decreased (television watching decreases activity)
B	Behavioural change—binge eating
C	Constitutional
D	Diet (fat-rich diet) Drugs—steroids, tricyclic antidepressants, oral contraceptives, valproate, phenothiazine and insulin will increase the appetite

E	Emotional factors Endocrine causes
F	Feeding habits—overeating, junk foods, foods with high glycaemic index (increases the blood glucose which stimulates insulin secretion)
G	Genetic—Prader–Willi syndrome, Laurence–Moon–Biedl syndrome, Beckwith–Wiedemann syndrome Glycogen storage disorder
H	Hereditary
I	Idiopathic



(a)



(b)

FIGURE 4.9 (a) An obese child. (b) Penis embedded in fat giving a false appearance of micropenis.

PARAMETERS

Ideal Body Weight

Ideal body weight is calculated as

$$\text{IBW (kg)} = 22.5 \times \text{height (m)}^2.$$

A child is classified as underweight, overweight or obese on the basis of IBW, as given in Table 4.24.

Weight

Classes of obesity according to the percentage of weight are given in Table 4.25.

Body Mass Index

The ratio between the weight and the height gives an idea of whether the weight is appropriate for the height.

$$\text{BMI} = \frac{\text{Weight (kg)}}{\text{Height (cm)}^2}$$

In children and adolescents, BMI more than 25 is considered obesity (Table 4.26).

BMI varies with weight and height of the child. For details, *see* Chapter 3.

TABLE 4.24 Grading of Nutritional Status According to IBW

Body Weight	Condition
Less than IBW by 18%	Underweight
More than IBW by 10%	Overweight
More than IBW by 20%	Obesity

TABLE 4.25 Classification of Obesity Depending Upon the Weight for Age

Classification	Weight (%)
Mild	120–130
Moderate	131–140
Severe	141–150
Very severe	> 150

TABLE 4.26 Classification of Nutritional Status According to BMI in Children and Adolescents

Classification	BMI in Children and Adolescents
Normal	15–22
Overweight	22–25
Obesity	> 25

Disadvantages of BMI in Assessing Obesity

- The shape and size of the body in children changes as they grow. This makes it difficult to assess the risk for obesity by BMI in children. It is difficult to interpret BMI during periods of rapid growth like puberty.
- It has a low sensitivity in identifying children with overweight and obesity.
- It does not distinguish between fat, muscles and bones. It may, therefore, give a false impression of obesity in large muscular children (mesomorphs). This is because their muscle mass will add to the weight but will not indicate their fat. BMI is normal in patients with sarcopenia (degenerative loss of muscle mass, strength and function) who have an increased percentage of fat and decreased muscle mass.
- Maturation pattern is different for boys and girls.
- BMI is not a direct measurement of body fat. Hence, percentage of body fat is considered to define obesity rather than BMI.

Skinfold Thickness

This indicates the status of fat deposits in the body. Harpenden caliper is used to measure the skinfold thickness. It is measured over the triceps, subscapular area, biceps and suprailiac area. Normal skinfold thickness depends upon the age and sex. This is more in females as compared to males. Values above 85 percentile in age-specific percentile charts are considered abnormal. Parameters of obesity are summarised in Table 4.27.

TABLE 4.27 Parameters of Obesity at a Glance

Parameters	Criteria
Body fat	Excess amount
Body weight	> 20% of the IBW
Weight for age	Above 120% of the standard weight > 2 standard deviations of NCHS standard
BMI	> 25 > 95th percentile for age and sex
Triceps skinfold thickness	> 85th percentile
Waist–hip ratio	> 0.8

Body Fat Percentage

- Normal values—in men, 15%–20%; in women, 25%–30%
- Deurenberg equation for adults:

$$\text{Adult body fat percentage} = 1.2\ (\text{BMI}) \times 0.23\ (\text{age in years}) - 10.8\ (\text{gender}) - 5.4$$

$$\text{Child's body fat percentage} = (1.51 \times \text{BMI}) - (0.70 \times \text{age}) - (3.6 \times \text{gender}) + 1.4$$

(Gender is 1 for males and 0 for females.)

Interpretation of body fat percentage is given in Table 4.28.

TABLE 4.28 Interpretation of Percentage of Body Fat

Significance	Percentage of Body Fat	
	Males (%)	Females (%)
Borderline obesity	21–25	31–33
Obesity	> 25	>33

TYPES OF OBESITY

1. According to the distribution of fat

Type	Areas of excess fat deposition
Generalised	Throughout the body due to overeating
Android	Chest and waist
Gynoid	Hips and thighs
Central	Face, neck and upper part of trunk—Cushing's syndrome

2. According to waist–hip ratio (Fig. 4.10)—waist-hip ratio is calculated as measurement at waist/measurement at hip. Waist is measured at the narrowest point between the rib cage and the iliac crest. Hip is measured at the maximal circumference at any point over the buttocks. Normal waist–hip ratio is 0.7. In obese children, it is more than 0.8. Types of obesity according to waist–hip ratio:
   - Pear-shaped—waist–hip ratio ≤0.8.
   - Apple-shaped—waist–hip ratio ≥0.9. This type is associated with more complications as compared to pear-shaped obesity.

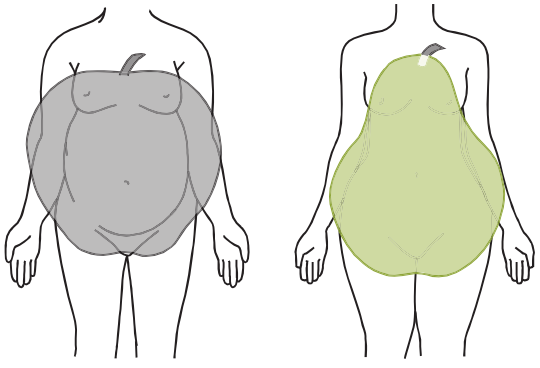


FIGURE 4.10 Apple- and pear-shaped obesity.

3. According to aetiology
   - Exogenous obesity
   - Endogenous obesity

   For details, see Table 4.29.

INVESTIGATIONS

- Thyroid function studies (hypothyroidism)
- Urinalysis—urine screening tests for mucopolysaccharidosis
- Plasma cortisol in suspected Cushing's syndrome
- Gonadal failure—testosterone, oestrogen, gonadotrophin levels
- Fat mass assessment can be done by CT scan, MRI, dual-energy X-ray absorptiometry, bioelectrical impedance analysis, body average density measurement, near-infrared interactance

TREATMENT

- Appetite suppressants—amphetamines, fenfluramine (not used in children); amino acids such as phenylalanine, tyrosine and tryptophan help curb hunger
- Behaviour modification

TABLE 4.29 Differences between Exogenous and Endogenous Obesity

Features	Exogenous Obesity	Endogenous Obesity
Predisposing factors	Excess diet consumption Decreased energy expenditure	Secondary to organic lesions
Causes	Constitutional Nutritional Decreased energy expenditure Increased intake (hyperphagia) Environmental causes Anxiety and depression	Genetic causes—Beckwith–Wiedemann syndrome, Laurence–Moon–Biedl syndrome, Prader–Willi syndrome, achondroplasia Endocrine—hypothyroidism, hypogonadism, Cushing's syndrome, growth hormone deficiency, hypothalamic and pituitary causes with voracious appetite (pituitary tumour, Frohlich's syndrome, craniopharyngioma) Pseudohypoparathyroidism, insulinoma, Mauriac syndrome—in cases with poor control of diabetes (obesity, short stature, hepatomegaly), precocious puberty, polycystic ovarian disease
Clinical features		
Fat distribution	Generalised	Buffalo hump
Height	Normal or tall	Decreased
Physical defects	Normal	Common—dysmorphic facies
IQ	Normal	Often low
Bone age	Normal or advanced	Often retarded
Blood pressure	Normal	Normal/increased
Endocrine changes	None	Acne Hirsutism Amenorrhoea Menorrhagia

- Diet—calorie intake reduced, junk foods should be avoided. Controlled weight loss (to reduce about 0.5 kg/week) should be aimed at
- Feeding habits—intake at regular intervals with no feeds in between
- Exercise
- Surgery—gastric and intestinal bypass surgery decreases the absorption of fat. Liposuction is done to remove the excess fat
- Health education and counselling—parental counselling and involvement is important

COMPLICATIONS

- Pulmonary—obstructive sleep apnoea, asthma, bronchitis, hypoventilation syndrome infections of respiratory system
- Gastrointestinal—gall stones (cholelithiasis), hernias (abdominal and inguinal)
- Cardiovascular—coronary artery diseases, atherosclerosis, increased tendency of clotting of blood, exercise intolerance, hypertension, varicose veins
- Orthopaedic—low backache, osteoarthritis, slipped capital femoral epiphysis, Blount's disease (tibia vara)
- Metabolic—dyslipidaemia
- Endocrine—diabetes mellitus type II, non-insulin dependent (with macrovascular and microvascular sequelae), hyperinsulinaemia
- Skin—intertrigo, acanthosis nigricans, furunculosis
- Life expectancy decreased, malignancies of endometrium, breast, prostate, colon, ovary; more prone for accidents
- Psychosocial problems, obesity in adult age, depression, effects on self-esteem and body image, withdrawn from peers, isolation, social discrimination, rejection by peers, reduced opportunity for school sports

PROGNOSIS

It is good for pear-shaped and exogenous obesity. Early diagnosis and preventive measures help prevent the complications. It may persist to adult obesity. Many children develop cardiovascular risk factors.

FAILURE TO THRIVE

Failure to thrive (FTT) is a condition where the growth of the child is much below the expected for that age or the child loses weight significantly over a short period of time. This term is used only for children up to 5 years of age. It is not a diagnosis but a term which is used to describe

- persistent weight loss,
- failure to gain weight (static weight), or
- fall in rate of growth from the child's normal percentile.

The child usually weighs below 3rd or 5th percentile, or the weight may decrease from 75th percentile to 25th percentile in a short time.

AETIOLOGICAL CLASSIFICATION

I. The causes are traditionally classified as follows:

1. Non-organic causes—these are responsible for up to 80% of cases of FTT. There is no known underlying medical abnormality. Poor growth is the result of following factors:
   - Psychosocial factors—emotional deprivation, child neglect and child abuse.
   - Poverty—inadequate food.
   - Lack of knowledge regarding feeding practices, food fads.
2. Organic causes—there is an underlying medical abnormality which is responsible for FTT in the child (Table 4.30). Gastrointestinal and neurologic diseases are most common organic causes of FTT.
3. Mixed—sometimes, both organic and non-organic causes coexist and play a role in decreased weight gain. This is common in children with cerebral palsy and multiple congenital defects.

II. Any condition that affects the intake, absorption and utilisation of the food will result in FTT (Table 4.31).

III. Classification according to intake of food—mostly, FTT is associated with low intake of food, but in conditions with increased metabolism, FTT occurs even with high intake of food.

TABLE 4.30 Organic Causes of Failure to Thrive

Classification	Causes
Cardiovascular disorders	Congestive cardiac failure, pulmonary arterial hypertension
Respiratory disorders	Cystic fibrosis, asthma, bronchiectasis, bronchopulmonary dysplasia
Gastrointestinal disorders	Malabsorption, inflammatory bowel diseases, pyloric stenosis
Neurological disorders	Cerebral palsy, mental retardation, CNS anomalies/tumours, degenerative disorders
Renal disorders	Renal failure, renal tubular acidosis, urinary tract infections, diabetes insipidus
Endocrine disorders	Hypopituitarism, hypothyroidism, diabetes mellitus, adrenal insufficiency, growth hormone deficiency
Chromosomal disorders	Down's syndrome, DiGeorge syndrome
Metabolic disorders	Inborn errors in metabolism, cystic fibrosis
Storage disorders	Mucopolysaccharidosis
Endocrine disorders	Hyperthyroidism, pituitary disorders, cretinism
Neoplastic disorders	Malignancy, CNS tumours
Infections/infestations	Tuberculosis, AIDS, infestation of GIT
Miscellaneous	Immunodeficiency disorders, collagen vascular disease, congenital defects like cleft lip/palate

HISTORY TAKING

Ideally, both parents should be present at the time of history taking and their interaction with the child and with each other should be assessed. The following history should be taken in a child who presents with FTT.

Age

- Common in infants and preschool children.

Sex

- Common in female children as they are not fed properly in certain communities, especially in rural areas.

TABLE 4.31 Causes of Failure to Thrive

Classification	Causes
Inadequate intake	Inadequate food—failure to provide adequate food or failure to consume adequate food Neglected child Decreased intake due to mechanical problems like cleft palate Cerebral palsy Vomiting due to various causes like metabolic disorders
Increased metabolism	Chronic infections Malignancy Hyperthyroidism Congenital heart disease
Problems in assimilation	Cystic fibrosis Celiac disease Intestinal parasitic infestation Portal hypertension Biliary tract disease Hepatic disorders—insufficiency Renal disorders—renal tubular acidosis, renal failure Storage disorders like glycogen storage disorder Galactosaemia Malignancy

Place

- Common in areas where the standard of living and earning capacity is low. Also, it is common in drought-hit areas.

Presenting Complaints

- H/o failure to gain weight adequately
- H/o loss of weight

History of Present Illness

- H/o inadequate intake of food
- H/o fever—infections, malignancy, collagen disorders causing increased metabolism and energy expenditure
- H/o fatty stools—fat malabsorption
- H/o diarrhoea—infections, malabsorption, chronic inflammatory bowel diseases

- H/o vomiting—gastro-oesophageal reflux, metabolic disorders, intracranial tumours
- H/o wheezing—asthma
- H/o loss of weight
- H/o loss of appetite—malignancy
- H/o recurrent respiratory infections—cardiac defects with left to right shunts
- H/o breathlessness—congestive cardiac failure
- H/o bleeding gums—leukaemia
- H/o swallowing problems
- H/o voracious appetite—lack of satiety seen in eating disorders, hyperthyroidism
- H/o PICA—worm infestation, mental retardation, iron deficiency anaemia
- H/o oliguria, anuria—renal problems
- H/o burning micturition—urinary tract infections

History of Past Illness

- H/o previous surgery
- H/o infections
- H/o cyanosis—cyanotic heart disease
- H/o recurrent respiratory infections—congenital heart disorders, cystic fibrosis
- H/o asthma
- H/o convulsions—neurological disorders
- H/o vomiting—metabolic disorders, CNS disorders

Antenatal History

- STORCH (syphilis, toxoplasmosis, other agents, rubella, cytomegalovirus, herpes) infections
- Planned/unplanned pregnancy

Neonatal History

- H/o prematurity, IUGR
- H/o birth asphyxia, neonatal convulsions
- H/o cyanosis—cyanotic heart disorders
- H/o recurrent vomitings—metabolic disorders

Immunisation History

Immunisation with measles vaccination to prevent measles

Growth and Developmental History

- Delayed milestones
- Mental retardation

Family History

- Number of children in the family
- Family history of similar illness—inborn errors of metabolism, infections, cardiovascular disorders
- H/o serious illness in the family
- H/o psychiatric illness or drug abuse in the family

Nutritional History

- Inadequate supply of food
- Inadequate intake by the child

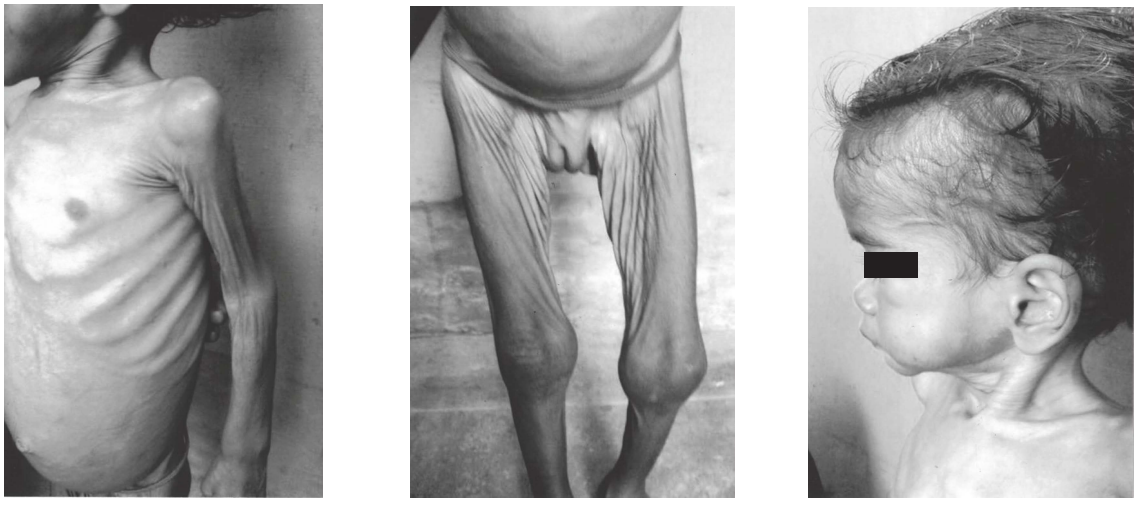
Socioeconomic History

- Poor hygiene
- Per capita income
- Education of parents

GENERAL EXAMINATION

Head-to-Toe Examination

- Hair—lustreless, hypopigmented
- Face—coarse facies in hypothyroidism, mucopolysaccharidosis
- Eyes—look for Bitot's spots, corneal/conjunctival xerosis and ulcer
- Oral cavity—delayed dentition, oral ulcers, glossitis
- Loss of subcutaneous fat (Fig. 4.11)
- Signs of vitamin deficiencies
- Skin infections
- Few physical signs may indicate the lack of care or neglect of the child. Look for dirty nails, flat occiput, intertrigo, alopecia areata on the posterior part of the scalp due to lying on the bed for a prolonged time. Also, look for features of child abuse.



(a) (b) (c)

FIGURE 4.11 Child with failure to thrive. (a and b) Note the wasting of muscles and loose folds of skin. (c) Buccal pad of fat is present. It is the last to be lost.

Vital Signs

- Temperature—increased in infections
- Respiratory rate—increased in respiratory infections
- Heart rate—increased in fever and cardiac disorders
- Pulse rate—increased in cardiac disorders

Anthropometry

Anthropometry is helpful in identification and monitoring response to therapy in a child with FTT. The following measurements are usually taken:

- Weight—below expected for age
- Height—normal or decreased. In acute cases, the length or the height is normal. In chronic cases, both weight and height are decreased
- MAC—may be decreased
- Head circumference—normal or near normal. Microcephaly may be seen in severely malnourished children and children with CNS disorders
- Skinfold thickness—decreased

SYSTEMIC EXAMINATION

- Cardiovascular system—auscultate for murmurs
- Respiratory system—rhonchi in asthma
- Abdomen—look for hepatosplenomegaly which is associated with storage disorders. Abdomen may be distended in malabsorptive disorders
- Nervous system—look for mental subnormality, transillumination test

INVESTIGATIONS

Blood

1. Complete blood count
   - Macrocytic anaemia—vitamin B_{12} or folic acid deficiency in disorders of small bowel
   - Microcytic anaemia—iron deficiency, blood loss, chronic infections
   - Polycythaemia in cyanotic heart diseases, chronic lung diseases
   - Leucocytosis in infections
   - Neutropenia in bone marrow hypoplasia or infiltration
   - Thrombocytosis in neuroblastoma with secondaries
2. Blood urea, creatinine for renal failure
3. Erythrocyte sedimentation rate

4. Serum electrolytes—hyperkalaemia in renal failure, decreased bicarbonate in acidosis
5. Blood culture for infections
6. HIV screening

Urine

- Urine albumin increased in nephritis, nephritic syndrome
- Urinary deposits—red bloods cells in nephritis, pus cells in pyelonephritis, urinary tract infections
- Urine pH >6.5 in renal tubular acidosis
- Urinary specific gravity <1.010 in diabetes insipidus
- Urine amino acid screening tests for inborn errors in metabolism
- Urinary culture and sensitivity

Stool

- Stool for ova, cyst and occult blood
- Stool fat increased in steatorrhoea
- Stool pH <6 in disaccharide intolerance
- Stool for reducing substances in lactose intolerance

Radiological Studies

- Chest X-ray
- Barium swallow
- Echocardiogram
- CT scan brain
- Ultrasonogram

Other Tests

- Chromosomal analysis (Down's syndrome)
- Thyroid function tests
- Liver function tests
- Sweat chloride test for cystic fibrosis
- Tuberculin test
- Small bowel biopsy for inflammatory bowel disorders, malabsorptive disorders, enzyme analysis

TREATMENT

Treatment of a child with FTT includes the following measures:

1. Nutritional rehabilitation
   - Dietary management
   - Therapeutic trial with feeds adequate in calories, fluid and protein. The child should be reassessed after 2 weeks. The child should be monitored daily during this period
   - Provide solid food before liquids
   - Avoid forced feeding or punishment for refusal of feeds
   - Let the child decide the quantity and type of the food to be consumed
   - Provide food with high calories and proteins
   - Isodense feeds which supply 100 kcal/100 mL can be given
2. Treatment of the organic conditions
   - Antibiotics for infections
3. Management of psychosocial issues
   - Improve the support to the child from the family and friends
   - Problems between the parents like marital conflict should be solved by proper counselling
   - Change in environment

Indications for Hospitalisation

Hospitalisation is needed in the following cases:

- Severe cases of FTT
- Children not showing improvement with outpatient treatment
- Suspected child abuse
- Detailed evaluation of an organic cause

SEQUELAE

- Growth retardation
- Mental subnormality
- Social and emotional problems
- Behavioural problems
- Delinquency

PROGNOSIS

It depends upon the following factors:

- Age of onset—the younger the age of onset, the more are the complications.

- Duration of FTT—the prognosis is good if the duration is short.
- Predisposing condition—children with decreased nutritional intake improve with proper nutrition. Few children with psychosocial causes may gain weight, though slowly. Such children may develop antisocial behaviour.

PREVENTION

- Identification and counselling of high-risk families
- Identification and treatment of organic causes at an early stage
- Health education
- Prevention of infections and infestation

DEVELOPMENT OF A CHILD

Development refers to maturation of functions, which is a continuous process from conception to maturity. The sequence of development is same in all children and progresses in cephalocaudal direction. Developmental assessment is important to monitor the child and should be done in all children. Any delay in development should be viewed seriously and a cause should be identified and intervened accordingly. Normal development of a child depends upon the interplay of the following factors:

1. Physical factors:
   - Warmth and clothing—in the absence of adequate warmth, more energy is spent by the child to maintain his body temperature. This delays the development of motor and mental milestones.
   - Activity—it is a form of stimulus to the child's development. A child who is active develops better than the child who is less active.
   - Food—good quality food with adequate calories, proteins and vitamins is necessary for the normal development. A child with severe malnutrition shows delayed development, whereas a child getting balanced diet develops optimally.
   - Function of senses—normal sensory input is necessary for optimal development. For example, a child who can see normally learns to imitate other's activities.
   - Good health—it is necessary for healthy development. A sound mind lives in a healthy body. A child who suffers from frequent illnesses suffers from delayed development.
   - Poverty—a big family size in the setting of poverty affects child's development adversely. It is an important cause of development impairment.
2. Psychological needs—apart from the above physical needs, the child's development depends upon the following psychological factors:
   - Personal identity and self-respect—deals with the questions that arise about oneself. The questions that arise are what am I? Who am I? etc.
   - Affection and care—good affection and care have a positive influence on the development of the child. A big family size leads to division of attention of mother, resulting in inadequate care.
   - Role model—usually every child has a role model. It can be anyone within or outside the family. The role model has a great influence on the child. The child tries to imitate him and be like him in every aspect. Parents should see that the role model is a right person.
   - Play—adequate play helps the child to develop optimally.
   - Security—a child who is taken care of by the grandparents is found to be more advanced in development. As the grandparents spend more time with the children, the child feels more secure and also the child has more time and opportunity to learn from their experiences.
3. Stimulation at optimal age—the stimulus for development should be provided at the earliest for the child to develop normally. The concept of sensitive and critical periods should be taken into consideration. There is a sensitive period during development for learning; proper guidance and training at that particular point enhances the development of child.

- Sensitive period—it refers to that period during development when the learning in response to stimuli is easier.
- Critical period—it is that period after which the stimulus in any form may not induce an optimal response. For example, if complimentary feeding (weaning) is not started by 6 months, the infant will refuse to take weaning foods. A younger child is able to learn a new language, music or sports better than an adult or an older child.

4. Prenatal and perinatal factors:
   - Genetic makeup of parents—this includes intelligence quotient (IQ) of parents, attitude of parents, whether they are carrier or sufferers of genetic diseases, etc.
   - Metabolic diseases (e.g., phenylketonuria), genetic disorders, congenital anomalies (spina bifida, cleft lip and palate) and chromosomal abnormalities (Turner's syndrome) etc.
   - Maternal illness and infections
   - Maternal drug and radiation exposure during pregnancy
   - Multiple pregnancies
   - Maternal stress
   - Preterm/low birth weight
   - Hypoxia

PRINCIPLES OF DEVELOPMENT

Development is a complex process. However, there are certain basic principles of development. These are as follows:

1. Rate of development—the sequence of development is same in all children but the rate of development varies from child to child.
2. Pattern of development—development proceeds in a cephalocaudal direction. For example, head control precedes trunk control and is achieved by 4 months. This is followed by rolling over at 5 months and sitting with support at 6 months. Control of limbs occurs from proximal to distal direction.
3. Corresponding primitive reflex—corresponding primitive reflex should be lost before definite milestones are achieved. For example, asymmetrical tonic neck reflex is abolished before the child can roll over; the palmar grasp disappears before the mature pincer grasp is attained.
4. Mass activity to specific individual response—the baby has disorganised mass activity for any stimulus. This is replaced by more mature specific individual responses as the child grows older. For instance, a small infant moves all the limbs to show pleasure or displeasure, whereas a 5-year-old child just smiles or cries for a similar stimulus.

HISTORY TAKING IN A CHILD WITH DEVELOPMENTAL DELAY

Age

One should know the correct age to assess the development of a child. In the preterm babies, the corrected age should be used as the chronological age. The correction is not required after about 24 months of age.

Sex

Boys and girls differ in acquiring milestones. Development of hand–eye coordination is advanced in boys. Development of speech and language is advanced in girls.

Place

A child brought from remote areas who has no access to healthcare facilities will show delayed development.

Reliability of the Informant

Information from the mother is more reliable than others. However, many mothers deny the fact that their child is lacking in development. The reliability of source should therefore always be judged.

History of Present Illness

- H/o delayed milestones—all milestones are delayed in cerebral palsy, especially quadriplegic

type; motor milestones are delayed in muscular disorders; mental milestones may be normal
- H/o injury
- H/o constipation (hypothyroidism)
- H/o regression of milestones (degenerative disorders, tumours in the brain)
- H/o decreased scholastic performance (psychological factors, physical factors, sexual abuse, degenerative disorders, tumours in the brain, etc.)

History of Past Illness

- H/o head injury
- H/o fever with convulsions or altered sensorium—postmeningitic or postencephalitic sequelae
- History of contact with a known case of tuberculosis—tuberculoma, chronic illness

Prenatal and Postnatal History

The reason for developmental delay is usually identifiable as an insult in the intrauterine or perinatal period, or disease affecting neuronal pathways and myelination in a growing brain. This is ascertained by taking a detailed history with emphasis on prenatal and postnatal periods and the course of development. Table 4.32 lists the prenatal, neonatal and postnatal factors which cause developmental delay. Other history to be ascertained is as follows:

- H/o decreased intrauterine movements (hypothyroidism)
- H/o maternal hypothyroidism
- H/o fever with rash during pregnancy
- H/o delayed cry/preterm/multiple pregnancies/hyperbilirubinaemia

Nutritional History

H/o malnutrition should be asked as it predisposes to decreased mental functions and delayed motor milestones due to nutritional myopathy.

Personal History

This includes the school performance, dietary habits and relationship with other children of a child older than 7 years.

TABLE 4.32 Conditions which Cause Developmental Delay

Period	Factors Affecting Development
Prenatal	Genetic factors—gene disorders Parental factors—intelligence, personality, educational status, attitudes, age of parents Maternal factors—drugs and alcohol abuse, smoking, irradiation, malnutrition, sedation Maternal infections—STARCH (syphilis, toxoplasmosis, AIDS, rubella, CMV, herpes) Obstetric factors—breech presentation, pregnancy-induced hypertension, eclampsia, cord prolapse, multiple gestation, obstructed labour, prolonged labour (>24 hours), premature rupture of membranes (>24 hours), prolonged second stage of labour (>2 hours), quick delivery (precipitate labour), rupture uterus Incest (predisposes to genetic abnormalities) Relative infertility (longer than usual time for conception after marriage may be associated with abortions, misconceptions. The incidence of neurological abnormalities is high in these children.) Insult to the foetus—hypoxia, exposure to irradiation due to X-rays, drugs, toxins, etc.
Neonatal	Prematurity, birth asphyxia, kernicterus, hypoglycaemia, intracranial bleed, neonatal seizures, intracranial infections
Postnatal	Malnutrition, hypothyroidism, infections like meningitis and encephalitis, irradiation, environmental exposure to toxins like lead and mercury

Family History

- H/o similar illness in the family
- H/o mental retardation
- H/o neurological disorders (familial spastic paraplegia)
- H/o familial pattern of development—the development may be early or late in other family members. This can be normal and should be considered before coming to a conclusion that the child is having delayed development.

Social and Environmental History

History regarding social and environmental factors like poverty, social and emotional deprivation, child abuse, cognitive stimulation should be taken.

EXAMINATION OF A CHILD WITH DELAYED DEVELOPMENT

General Examination

- Look for features of chromosomal disorders like Down's syndrome.
- Look for features of hypothyroidism.
- Look for the abnormal signs (e.g. microcephaly, opisthotonus, hypo/hypertonia) which may be associated with delayed development.

Vital Signs

- Heart rate—decreased in hypothyroidism
- Pulse—slow in hypothyroidism
- Temperature—decreased in hypothyroidism

Anthropometry

- Weight—decreased in malnutrition
- Height—decreased in chronic malnutrition, chromosomal abnormalities like Down's syndrome
- Head circumference—decreased in Down's syndrome and hypothyroidism
- Midarm circumference—decreased in malnutrition

Neurological Signs

Soft neurological signs are present in normal children during various stages of neurodevelopment. This depends upon neural maturation. The signs are abnormal when they are present at an age when they are not supposed to be present. These are motor or sensory tests which are abnormal for particular age (Table 4.33). Abnormalities in the development or maturation of the nervous system of a child are usually missed while examining a case with neurological illness.

Soft neurological signs are associated with abnormal development or maturation of the CNS of the child. The following factors are associated with soft neurological signs:

- Poor motor coordination
- Sensory perceptual difficulties
- Difficulty in sequencing of complex motor tasks
- Diffuse brain structural abnormalities

Presence of two or more soft neurological signs is significant. These are present in neurological disorders like cerebral palsy and attention deficit disorders.

Hard neurological signs are behavioural signs that always reflect brain injury. These include seizures and cranial nerve abnormalities leading to deafness, blindness, etc.

TABLE 4.33 Soft Neurological Signs

Type	Soft Neurological Signs
Poor fine motor coordination	Finger tapping, dressing, undressing, rapid alternate movements
Special senses	Tactile localisation test
Laterality	Ask the child to show the right hand, left eye, etc.
Orientation in space	Touch the thumb with index finger

DEVELOPMENTAL SCREENING

It refers to checking a group of children or a large population by trained personnel at appropriate ages. Every health contact with the child should be used to check that development is progressing normally. Denver Developmental Screening Test is a reliable method to pick abnormalities at an early stage.

DEVELOPMENTAL ASSESSMENT

It refers to a detailed analysis of either specific areas of development or overall development. Every child should be assessed periodically for normal development. For this, one should be aware of the age at which a normal child can perform certain activities like climbing stairs, throwing balls, etc. For preterms, the corrected age should be taken as the chronological age till about 2 years.

Development is intimately related to the maturation of nervous system. Delay in achieving a single milestone need not imply mental retardation but gross developmental delay is highly indicative of mental retardation. Various developmental assessment tests in use are Griffiths and Bayley Infant Development Scales, Reynell Language Scale, etc. (Table 4.34).

TABLE 4.34 Developmental Assessment Tests

Test	Method	Age Group
Gesell's Developmental Schedule	Measures four functional areas of development	For children aged 4 weeks to 3 years
Bayley Scale of Infant Development (BSID)	67 motor tests	Children aged <2 years
Denver Developmental Screening Test (DDST)	Four areas of development	0–6 years of age
Vineland Social Maturity Scale	Measures about 117 items like social competence, self-help skills, adaptive behaviours, personal and social skills like daily living skills, communication, socialisation, occupational skills	For children from birth to adulthood (30 years) Classroom version 3–12 years
Seguin Form Board	Assesses visual discrimination and matching eye–hand coordination using 10 differently shaped blocks and a large board recessed corresponding to these shapes. The child is asked to place the blocks fastly. Three trials are given and time is noted. The time and number of errors are noted.	3½–10 years (<16 years) Girls perform better than boys
Trivandrum Developmental Screening (TDSC)	17 simple tests from Bayley Scales of Infant Development	<2 years
Baroda Development Screening Test (BDST) Phatak's Baroda screening test	Uses 22 motor items and 31 mental items. It is adapted from Nancy Bayley Development Scale for children.	Birth to 30 months (monthly up to 12 months and every 3 months up to 30 months)
Brazelton Neonatal Behavioural Assessment Scale	The baby's 28 behaviour items and 18 primitive reflexes are observed	Newborn baby

AREAS OF DEVELOPMENT

There are five areas of development according to the functional skills. These are as follows:

- Gross motor
- Fine motor
- Speech and language
- Social development, adaptive skills and general understanding
- Hearing and vision

If either of these is affected, it affects the development of another skill. For example, a child with defective vision will have abnormal social skills.

Gross Motor Skills

The baby is assessed for gross motor development in the following positions:

- Ventral suspension—up to 3 months of age. The newborn baby is suspended in prone position with a hand placed under the chest
- Supine position—lying down with face upwards
- Prone position—lying down with face downwards
- Sitting
- Standing

Assessment in the First 3 Months

The infant less than 3 months should be examined by holding in ventral suspension, prone, supine and sitting positions. Developmental assessment in the first 3 months of life is given in Table 4.35 (also see Fig. 4.12). After 3 months, ventral suspension is not used to assess the head control of the normal babies.

Assessment between 3 and 12 Months

Gross motor developmental assessment between 3 and 12 months is done in prone, sitting and standing positions, as given in Table 4.36 (also see Fig. 4.13).

TABLE 4.35 Developmental Assessment in the First 3 Months of Life

Age	Ventral Suspension	Prone	Supine	Pull to Sit
Birth	Complete lack of head control. Term baby has a straight back, with elbow and knees flexed and slight extension at hips. Preterm babies are hypotonic and hang limply	Head turned to one side. In term babies, pelvis remains high up with knees drawn up under the abdomen In preterm babies, the hip will be abducted and flexed; pelvis will not be high	Asymmetric tonic reflex present at rest	Complete head lag. Back is rounded in sitting posture
6 weeks	Lifts and momentarily holds the head in the same plane as rest of the body	Lifts the chin above the ground momentarily. Hips and knee partially extended	Asymmetric tonic reflex present intermittently at rest	Head lag decreases
8 weeks	Can maintain the head in the same plane as the rest of the body	Head in the midline. Lifts the chin intermittently so that the plane of the face is at 45° to the couch	Asymmetric tonic reflex present intermittently at rest	Less head lag
3 months (12 weeks)	Lifts and maintains the head well beyond the plane of the body	Lifts and holds the chin and shoulder off the couch for prolonged periods so that the plane of face is between 45° and 90° to the couch. Legs are completely extended. Weight borne on forearms	Asymmetric tonic reflex will be absent	Head lag slight. Holds the head erect, but it remains unsteady



(a) (b) (c)

FIGURE 4.12 Gross motor milestones (birth to 3 months). (a) Ventral suspension: 6 weeks—head held in same plane as rest of the body. (b) Ventral suspension: 3 months—head held beyond the plane of rest of the body. (c) Prone: 12 weeks—weight on forearms, plane of face almost 90° to couch.

Assessment after 12 Months

The age at which the child acquired various milestones should be enquired. When did the child attain the following milestones—head control, sitting with support/without support, standing with support/without support, walking with support/without support?

The milestones, which the child should have attained by the corresponding age, are given in Table 4.37.

Fine Motor Skills

These include advanced hand skills, hand–eye coordination, hand–mouth coordination, etc. Manipulation of things using the hand should be observed. The infant observes his hands intently between 12 and 20 weeks. This is called hand regard. Table 4.38 gives the normal age of attainment of fine motor skills (see also Figs. 4.14 and 4.15). These skills can be tested by using various methods like ability to use cubes, writing, feeding, dressing, etc.



(a)



(b)



(c)



(d)



(e)



(f)

FIGURE 4.13 Gross motor milestones (older than 3 months). (a) 11 months—creeps (abdomen off the couch). (b) Pull to sit: 4 months—no head lag. (c) Sitting position: 16 weeks—back much straight. (d) 11 months—pivoting, turns around to pick an object. (e) 11 months—can stand holding onto furniture, can walk holding onto it (cruises). (f) 13 months—walks without help with broad base, flexed elbows, abducted arms, steps of unequal length and varying direction.

TABLE 4.36 Gross Motor Developmental Assessment between 3 and 12 Months

Age (Months)	Prone	Sitting	Standing
4	Chest is maintained off the couch so that the plane of face is at an angle of 90° to the couch	The baby holds the head steadily. No head lag. If the head is rotated, the head control will disappear. Back is much straighter and curved only in the lumbar region	Not tested
5	Supports own weight on forearm and lifts the upper part of the body above the ground	Head position is not disturbed by sudden rotation	Not tested
6	Supports own weight on hands with extended elbows Rolls over from prone to supine	Can sit with own support Can sit momentarily without support	Bears some weight on the legs when holding the baby in standing position
7	Rolls over from supine to prone	Can sit without support for few minutes	Bears full weight on the legs Bounce on standing
9	Crawls on abdomen	Can sit steadily without support and can lean forward	Pull to stand
11	Creeps (abdomen off the couch)	Sits up from supine position Pivots (turns the back sidewards by twisting to pick an object from behind)	Walk with support holding on to furniture (cruises) Can cruise holding a furniture
12	Walks on hands and feet like a bear	Pivots and manipulates several things around him	Walks with one hand held

Testing by Cubes

For the purpose of testing, several 1-inch cubes are used. Testing an infant by the ability to grasp and use cubes is given in Table 4.39 (also see Fig. 4.16). A slightly older child can be tested by the ability to make a tower of cubes. The number of cubes used to build the tower should be noted. The imitating and copying skills of the child can also be tested using cubes. First, the child imitates and then copies. Imitation is an advanced behaviour where an individual observes and replicates another's act. Copying is a reproduction of a written record. (*Remember—**I**nitially **I**mitates **Co**nsequently **Co**pies.*)

Drawing and Writing Skills

The child can be tested for fine motor skills by asking to write with a pencil. Table 4.40 gives various drawing skills at different ages (Fig. 4.17). The child develops vertical stroke by 18 months and then horizontal stroke. (*Remember—When we write the letter 'L' first we make a vertical stroke and then horizontal.*)

Goodenough Draw-a-Man Test

This test is done for a child between 3 and 10 years. Ask the child to draw a man. Count the number of parts drawn by the child like head, legs, arms and trunk. Scoring is given as follows:

Score	Number of parts drawn
1	One (e.g., head present)
2	Two (e.g., head and legs present)
3	Three (e.g., head, arms and trunk present)

For each 4 points, add 1 to the basal age which is 3 years. For example, if the child draws 6 items, add 1½ to the basal 3 years. Hence, the mental age of the child will be 4½ years.

Feeding Skills

The ages at which the child develops various feeding skills are given in Table 4.41.

Dressing Skills

The ages at which the child develops various dressing skills are given in Table 4.42.

Handedness and Skills to Use a Book

Handedness evolves by 2 years and gets established

TABLE 4.37 Age of Attainment of Gross Motor Skills after 12 Months

Age	Gross Motor Milestones
13 months	Walks without support with broad base and unequal steps Walks independently without help
14 months	Walks sidewards Walks backwards
15 months	Walks well without support Creeps upstairs Kneels with no support Will not stop suddenly
18 months	Running Creeps steps upwards and downwards Carries toy while walking (walks carrying a doll) Seats self on a chair Jumps with both feet
2 years	Walks upstairs with 2 feet per step Walks backwards in imitation Picks up object (without fall) Walks, climbs and runs Can climb up and come downstairs alone Kicks ball without losing balance
2½ years	Jumps with both feet
3 years	Can ride a tricycle (cycle with 3 wheels) Walks forwards, backwards, sidewards (3 ways) Can climb upstairs with alternating steps in adult manner Comes downstairs with two feet per step Walks, runs, climbs, kicks and jumps easily Can run and turn around obstacles Stands momentarily on one leg
4 years	Stands with one leg Can come downstairs one step at a time (with alternating steps) Can hop on one foot Can skip on one foot Can turn without loosing balance
4–5 years	Can climb a tree Can catch a ball
5 years	Skips with both feet Jumps off three steps

by 3–4 years. Infant has bidextrous grasp. The child can be tested by asking to use a book. These are given in Table 4.43.

TABLE 4.38 Age of Attainment of Fine Motor Skills

Age	Fine Motor Skills
1 month	Hands remain closed
1.5 months	Hands often open
2 months	Hands frequently open, slight grasp reflex
3 months	Primitive grasp reflex disappears and the child opens hands spontaneously
4 months	Grasps objects placed in his hand with ulnar aspect (ulnar grasp) Hands comes together in midline (like pray) Hand regard Child reaches for a dangling ring held in front with both the hands (bidextrous approach) Tries to reach for object, but overshoots Can take foot to opposite knee
5 months	Grasps objects voluntarily with both hands Plays with toes/feet Takes feet to mouth
6 months	Reach for an object with one hand (unidextrous approach) Holds objects with crude grasp from palm (palmar grasp) Drops one cube when another is given
7 months	Transfers objects from one hand to other Retains the first cube in hand when second is offered Bangs cube on table
8 months	Intermediate grasp of a cube Tries to reach for toys or cubes out of reach
9 months	Palmar grasp obliterated Immature pincer grasp—picks things up with thumb and index finger Matches cubes by bringing them together
10 months	Index finger approach Finger–thumb apposition Can put an object (pellet) into bottle Begins to release objects
11 months	Uses index finger to poke at objects Puts cubes in and out of container
12 months	Mature pincer grasp of a cube Can release object on command Throws object on floor Holds 2 bricks and bangs Holds objects such as a spoon and cup
13 months	Can turn 2–3 pages of a book at a time (>1–3 pages)

(Table continued)

TABLE 4.38 *(Continued)*

Age	Fine Motor Skills
15 months	Can drink from a cup Can feed without help Can feed self with spoon with spilling Can imitate scribble Can build tower of 2 cubes Can hold 2 cubes in 1 hand
18 months	Can copy vertical stroke Feeds self with spoon without spilling Can build tower of 3 cubes
2 years	Can build a tower of 6 cubes Books—turns one page at a time Scribbles if given a pencil or crayon Begins to eat by himself or herself Imitates vertical/horizontal stroke Puts and takes off shoes and socks
2.5 years	Picks up thread Can build a tower of 8 cubes Turns pages singly
3 years	Can dress and undress himself Can build a tower of 9 cubes Imitates bridge Can copy a circle Can cut with scissors Can pull a large toy
4 years	Can copy a cross or square Can copy a bridge Imitates a construction of gate with 5 cubes Can draw a man with 4 parts
5 years	Can throw accurately Can copy a triangle Can catch a ball Can tie the shoe lace
6–7 years	Can copy a diamond
7 years	Kite
8 years	Double-lined cross
9 years	Copies a cylinder
11 years	Can copy cube

TABLE 4.39 Testing of Fine Motor Skills by Use of Cubes

Age	Fine Motor Skills
4 months	Tries to reach for the cube, but overshoots and misses Child reaches for an object with both the hands (bidextrous approach)
5 months	Can grasp objects voluntarily with both hands
6 months	Unidextrous approach Palmar grasp Drops one cube when another one is given
7 months	Bangs cube on the table Transfers cube from one hand to the other Retains the first cube in hand when second is offered
8 months	Tries to reach for toys or cubes out of reach Intermediate grasp of a cube
9 months	Matches cubes
10 months	Index finger approach Begins to release objects
11 months	Puts cubes in and out of the container
11–12 months	Mature grasp of cube Throws cubes on the floor
12 months	Mature grasp of cube Throws cubes on the floor (casting) Attempts tower of 2 cubes
15 months	Can build a tower of 2 cubes Casting stops
18 months	Can build a tower of 3 or 4 cubes
2 years	Can build a tower of 6–7 cubes Imitates train of cubes, without adding chimney
2.5 years	Can build a tower of 8 cubes Imitates train of cubes, adding chimney
3 years	Can build a tower of 9 cubes Imitates bridge
3.5 years	Can build a tower of 10 cubes Copies bridge
4 years	Imitates GATE
4.5 years	Copies gate
5–6 years	Can make STEPS

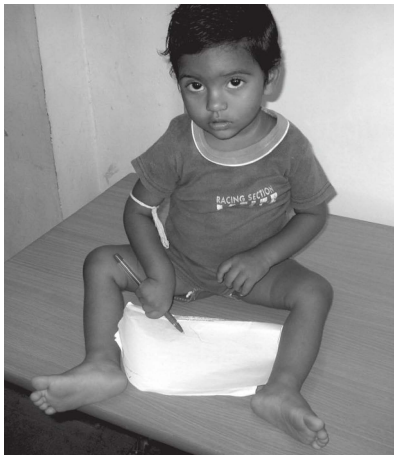
Imitating: If a child observes someone drawing an object, he imitates.

Copying: If a child draws an object after seeing a completed drawing, without observing how it is being drawn, he copies.

Speech and Language

Speech is use of words. Language is expression of thought in words. Vocabulary is amount of words. The age at which the child speaks varies from one child to other. Various factors play a role in the development of speech. These are as follows:

- Anatomical defects—cleft lip and palate result in indistinct speech.
- Environmental—when the child is overprotected, he does not feel the necessity for communication; hence, speech development is delayed.



(a)



(b)



(c)

FIGURE 4.14 Fine motor milestones. (a) 15 months—scribbling. (b) 15 months—feeds self with spoon with spilling. (c) 2 years—puts and takes off shoes and socks.

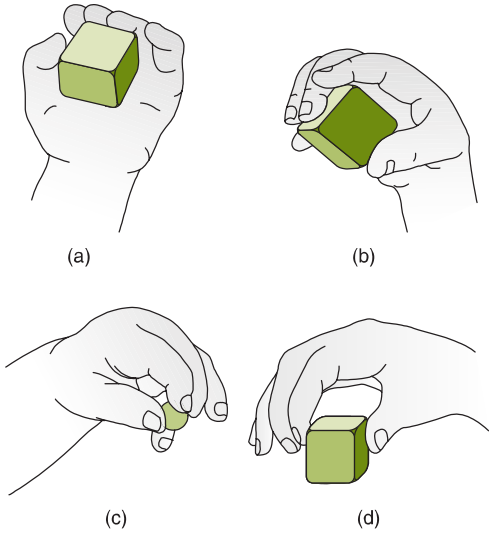


FIGURE 4.15 (a) 6 months—immature palmar grasp. (b) 8 months—intermediate grasp. The child begins to use the radial aspect of hand. (c) 9–12 months—pincer grasp. (d) 1 year—mature grasp.

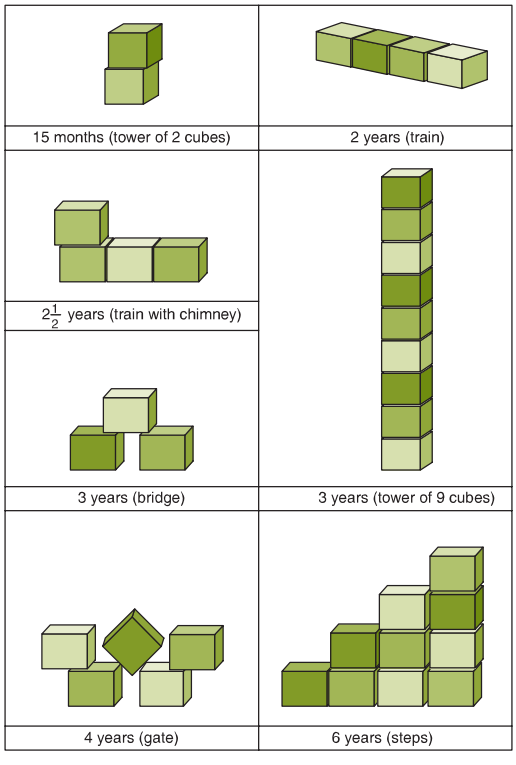


FIGURE 4.16 Testing fine motor skills with the help of cubes.

TABLE 4.40 Drawing and Writing Skills at Various Ages

Age	Development of Writing/Drawing Skills
15 months	Can imitate scribble
18 months	Makes strokes imitatively Spontaneous scribble
2 years	Imitates vertical strokes Imitates circular strokes Can copy a line (vertical first and then horizontal)
2.5 years	Holds pencil in hand instead of fist Imitates horizontal stroke Makes two or more strokes for cross Imitates 2–3 lines
3 years	Can copy a circle Imitates cross
4 years	Can copy a cross
4.5 years	Can copy a square
5 years	Can copy a triangle
6 years	Can copy a hexagon
7 years	Can draw a kite Can draw a diamond
8 years	Double-lined cross (cross with two lines)
9 years	Copies a cylinder
11 years	Copies a cube

TABLE 4.41 Feeding Skills at Various Ages

Age	Development of Feeding Skills
4–5 months	Drinks from cup when held to lips
6–7 months	Can hold a bottle and drink Chews Feeds self with biscuit Can hold a spoon
15 months	Can feed self without help (picks cup, drinks, puts it down) Feeds self with spoon with spilling
18 months	Can feed self by spoon without spilling
2.5–3 years	Cut and eat with knife and fork

- Familial factors—if parents are not intelligent, the speech of the child will be delayed. There may be a similar history of delayed speech in family members. This is due to delay in maturation of the part of the nervous system concerned with development of speech.

TABLE 4.42 Dressing Skills

Age	Development of Dressing Skills
1 year	Child can make postural adjustment for dressing Can pull off mittens and caps
1.5 years	Unzips Fumbles with buttons
2 years	Puts and takes off shoes and socks
3 years	Can dress and undress self fully if helped with buttons and advised about correct shoe (dresses on own)
5 years	Ties the shoelace Fully independent

TABLE 4.43 Skills of a Child for Using a Book

Age (months)	Book-Related Skills
15	Shows interest in books
18	Turns pages in bunches—2–3 pages of a book at a time Points to picture—car, dog, cat
24	Turns 1 page of a book at a time

Remember 1 and 2. 1 year—2 pages at a time; 2 years—1 page at a time.

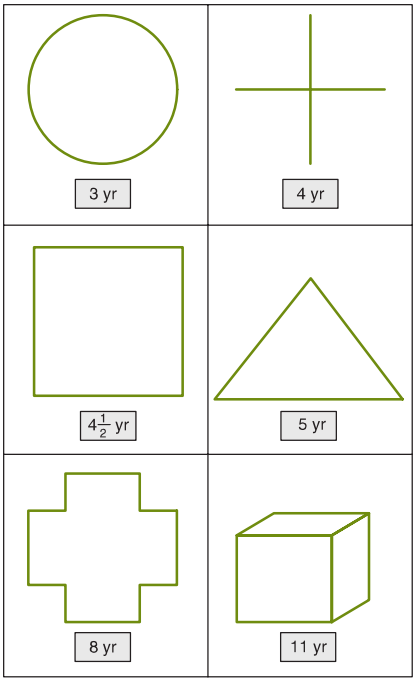


FIGURE 4.17 Drawing skills at various ages.

- Genetic factors—genetic defects are associated with neurological handicaps.
- Gender—girls begin to speak earlier than boys. The amount of word output is more in girls than boys of same age group.
- Hearing defects—if hearing is absent, the child does not develop speech (deaf-mutism). If the hearing is defective, the speech development will be poor.
- Intact nervous system—damage to the speech centre results in motor, sensory or conductive or global aphasia.
- Early stimulation—babies who are talked to develop speech earlier than babies that are not taken care of.

The development of speech and language in a normal child is given in Table 4.44.

Social Development, Adaptive Skills and General Understanding

The social and adaptive skills develop as a response of the child to environment and to others. These are summarised in Table 4.45. For the first 6 months, the infant is dependent on the mother. After 6 months, the infant tries to explore the environment in the process of becoming independent. The child develops communication skills which can be verbal or non-verbal. Non-verbal communication is done by gestures and includes smiling, vocalising in response, turning the head away, placing the hand on the object the child wants or directing fingers at it, temper tantrums (throwing away objects or kicking at an object in anger) etc. Verbal communication is done by using words and has been already explained. Infants are not apprehensive until 7 or 8 months of age. Only after 7 months of age the child develops a period of negativism. Most infants under 7 months of age actually enjoy examination by the clinician. (*Remember—First year: imitates mother, one person [first person]; Second year: imitates mother and others, i.e., two or more persons [second person].*)

Bladder and Bowel Control

The age at which the child attains bladder and bowel control depends on the training and conditioning of the child. Micturition is a reflex act in the newborn

TABLE 4.44 Development of Speech and Language

Age	Speech and Language
1 month	Small throaty noises, turns head to sound
2 months	Smiles and vocalises when talked to
3 months	Squeals with pleasure (cooing sounds)
4 months	Laughs aloud
5 months	Razzing, *Ah–ooh*
6–7 months	Monosyllables (*Ma*, *Ba*)
8–9 months	Repetition of consonants Combines syllables—mama, dada (*ma ma*, *da da*) Imitates sounds
10 months	Speaks 1 word with meaning Says no
12 months	Speaks 1–2 words with meaning Tries to imitate words
13 months	2–3 recognisable words
14–15 months	2–6 recognisable words Can name a familiar object (pencil)
15–16 months	Childhood jargon Can name pictures
18 months	Many intelligible words Speaks at least 6 words. Uses 6–20 recognisable words (about 18 words) Points to eye, nose, ear Attempts to sing a song
2 years	Says simple 2-word sentences *Remember—Simple Sentence: Second Year S S)* Repeats things said Uses me, I, you Speaks 50 or more words Understands 120–175 words Points to at least one part of the body
2.5 years	Joins in nursery rhymes and sings Puts 2–3 words into simple sentences Phrases of 2–3 words Asks names of objects/people Uses pronouns, prepositions Understands 400 words
3 years (in 36 months)	Good vocabulary of 250 or more words Understands 800 words, uses plurals Asks questions 3–6 word sentences Knows own full name, sex, age Counts 3 objects correctly Repeats 3 numbers Repeats a sentence of 6 syllables Understands numbers (1, 2, 3, … etc.)

(Table continued)

TABLE 4.44 *(Continued)*

Age	Speech and Language
3.5 years	Understands 1500 words Good vocabulary Uses 6-word sentences Can narrate events Names 4 colours
4 years	Knows 2–4 parts like face, head, nose Can count 4 coins correctly Describes and gives account of recent experiences Can tell long stories Asks meaning of new words
5 years	Speaks at least 10-word sentences Can repeat a sentence of 10 syllables Counts 10 coins correctly Uses longer sentences Counts up to 10 Can say address Can say (telephone) number Answers simple questions Can speak in sentences and uses many different words Addition within 5 like 2 + 3 = 5
6 years	Understands 2500–2800 words Names at least 4 colours Grammatical speech Meaning of abstract words Counts up to 20 Repeats weekdays
7 years	Names weekdays (7)
8–10 years	Can count 6 digits forwards Can describe abstract things
10–12 years	Uses telephone directory Reads a story Writes letter on his own

period. Bowel control is usually achieved before the bladder control. It is important to note when the child attained the bladder and bowel control for day and both for day and night. Bowel control is usually attained by the age of 18 months. Bladder control for daytime is usually achieved by 1.5–2 years (Table 4.46). Bladder control for both day and night is achieved by the age of 3 years in 75% of the children. Ninety per cent of the children are dry during both day and night by 5 years.

TABLE 4.45 Social and Adaptive Skills

Age	Social and Adaptive Skills
4 weeks	Looks at face when spoken to (face regard)
6–8 weeks	Smiles and vocalises when spoken to (social smile). This is different from spontaneous smile present in neonates. (*Remember—**S**econd month **S**ocial **S**mile [**S S S**]*)
12 weeks	Hand regard Recognises mother Shows interest in surroundings (fan, toy, etc.) Anticipates food
16 weeks	Laughs loud Shows massive reaction involving all 4 limbs on excitement Shows pleasure when pulled to sitting position Can turn his head when called
6 months	Imitates cough Shows likes and dislikes Distinguishes the difference in friendly/angry voice Smiles at the mirror image Stranger anxiety Will stretch arm when mother tries to lift
7 months	Period of negativism (resists things being taken away) Separation anxiety Can imitate (putting the tongue out, laughing)
8 months	Responds to own name Enjoys peek-a-boo games Looks for dropped toy
9 months	Less dependent on the mother Waves bye-bye Plays pat-a-cake Attention seeking activities Laughs when laughed at Will pull the cloth of the mother
10 months	Deliberate dropping of things
12 months	Comes when called Can play a simple ball game Throws objects on floor Feeding—attempts self Anticipates body movements when nursery rhyme is being said Enjoys playing Enjoys clapping
15 months	Feeds self—no help needed, manages a cup May kiss pictures of animals Follows simple commands—may kiss on request Bladder—will indicate wet pant Mimics others' actions Domestic mimicry imitates the mother (sweeping washing), imitates dusting and washing, mimics cleaning, imitate sweeping

(Table continued)

TABLE 4.45 *(Continued)*

Age	Social and Adaptive Skills
18 months	Tells mother about wetting Points to parts of body like ear, nose on command Responds to surrounding environment/people Shows feelings of jealousy and affection Shows sustained interests Explores environment Dry by day—Tells (mother) about wetting
2 years	Becomes more independent Wants to be independent, resists being fed or dressed by the mother (second person) Says no to most of the things asked for Mostly dry by day Wears simple garments (**s**ocks, **s**hoes) Temper tantrum Plays alone Points to objects when named Points to picture when named (e.g., nose, eyes) Enjoys simple stories/songs Imitates others' behaviours Wraps up doll and put it to bed Parallel play—plays near others watching them Pulls people to show them toys
2.5 years	Plays alone Pulls down pants at toilet but can not replace
3 years	Can say the age, sex Can say his name Can identify 3 basic colours (red, blue and green) Goes to toilet unassisted—bladder control—dry by night also Mature pen grasp Obeys triple order (go to dining room, open the fridge, take the water bottle) Shows affection for younger siblings Uses make-believe objects in play Matches or names 2 or 3 primary colours Washes hands but needs supervision Can pull pants down and up but needs help for buttoning Shares, plays with others Listens eagerly to stories Recognises and identifies common objects and pictures
4 years	Can wash face Matches 4 colours
5 years	Domestic role play Group activities Understands opposites—right and wrong (e.g., fat and thin, tall and short) Washes hands without supervision

(Table continued)

TABLE 4.45 *(Continued)*

Age	Social and Adaptive Skills
5–6 years	Shows interest in sports and study (academic) activities
7 years	Knows morning, evening Knows the colour orange
7–8 years	Shows interest in members of same sex
8–10 years	Takes care of household activities like looking after the young child Fond of judgement and experience Can describe abstract things
10–12 years	Assumes responsibility for household care

TABLE 4.46 Bladder Control

Age	Bladder Control
15–18 months	Says when he/she is wet
18 months–2 years	Dry by day
2.5 years	Climbs onto lavatory seat
3 years	Dry by day and night
4 years	Attends to own toilet needs

Hearing and Vision

Hearing

The baby responds to sound differently according to its age. Normal response to sounds at different ages is given in Table 4.47. To test hearing in a baby, make a sound at about 18 inch from the ear. In children with hearing impairment, take the history of the following high-risk factors:

- H/o infections—meningitis, mumps, measles
- H/o head injury
- Ototoxic drugs—kanamycin, streptomycin, gentamycin
- H/o infections like rubella in mother
- H/o low birth weight, birth asphyxia, jaundice/kernicterus/exchange transfusion, etc.
- H/o delay in speech and language
- Family history of hearing problems

Look for external ear abnormalities. Also look for the following conditions which may be associated with hearing problems:

- Recurrent middle ear infection
- Pierre–Robin syndrome
- Waardenburg syndrome

TABLE 4.47 Developmental Assessment of Normal Hearing

Age	Response to Sound
Newborn	Startle reaction Blinking Facial grimace Change in heart rate
3–4 months	Turns the head to the side of the source of sound and the eyes look to the same side
5–6 months	Turns to one side and then looks down if the source of sound is below the level of ear
6–7 months	Turns to one side and then looks upwards if the source of sound is above the level of ear Can imitate sounds
7–8 months	Turns the head in curving arc towards the source of sound Can respond to name
8–10 months	Turns the head diagonally and directly towards the source of sound
11–12 months	Localises the sound source like adult

Vision

The development of normal vision in a baby should be observed from the newborn period (Table 4.48). The newborn baby responds to changes in illumination and can fixate its eyes to points of contrast. Any delay in the normal development should be evaluated and corrected at an early stage to prevent visual defects.

Visual Acuity and Vision Testing. Visual acuity is the resolving power of the eye. It is the ability to distinguish letters and numbers at a given distance. It refers to the sharpness of vision. It should be tested when the child develops the ability to name, copy or match letters or numbers. It is tested by Snellen chart in children after the age of 3 years.

Visual acuity depends upon how accurately the light focuses on the retina. It should be tested in each eye separately. The normal visual acuity is 20/20 (if the distance is measured in feet) or 6/6 (if the distance is measured in metres). The numerator is the distance from which the child can reliably distinguish the letters. The denominator is the distance from which an adult with normal eyesight can reliably distinguish the letters.

TABLE 4.48 Various Stages in Development of Normal Vision

Age	Features
From 36 weeks of gestation onwards	Optokinetic nystagmus present
Soon after birth	Fixation reflex may be seen. In response to a visual stimulus, the baby will demonstrate monocular fixation and generalised diminution of the bodily activity. Term babies can fix and track an object held 20–30 cm away from the face with difficulty. Differentiates between light and darkness. On flashing a bright light on the baby's eyes, there will be frowning, blinking of the eyelids and contraction of the orbicularis oculi muscle. The pupillary reflex will be present.
4 weeks	Infant can follow an object up to 60° on each side of the midline.
5–6 weeks	Binocular vision begins. The infant will also have prolonged visual contact with the adult.
2 months	The infant will follow the objects or the mother
3 months	Hand regard (3–5 months). Can follow an object through an arc of 180° Increased coordination of eye movements resulting in convergence of both eyes.
4 months	Binocular vision is well established. Some perception of colours will begin.
5–6 months	True coordination of the eyes and hands begin to appear.
3 years	Infant can identify the basic colours. Formal vision screening should be done at the age of 3 years by using an illiterate 'E' chart. The 'E' chart is printed with letter E, with the bars up, down or facing right or left. The other cards used are Allen picture cards, LH flash cards, HOTV letter matching test.
After 7 years	Titmus fly test for stereoacuity

From optical perspective, 20 feet is essentially infinite; 20/20 is the visual acuity needed to discriminate two points separated by 1 arc minute (about 1/16 of an inch) at a distance of 20 feet. Visual acuity of 20/40 is considered half the normal and 20/10 is twice the normal acuity. In a normal emmetropic eye, maximum visual acuity can be 20/16 or 20/12 only.

Place the chart at 20 feet or 6 m and illuminate to 480 lux. With the occluder placed before one eye, test the other eye. After testing the visual acuity for distant vision, test the acuity for near vision with Jaeger's chart. After testing both the eyes separately, test both eyes together as the binocular visual acuity is better than monocular acuity. The visual acuity in the newborn is 20/400. By 5–7 years of age, it becomes 20/20. Macular development is complete by the age of 5–7 years only. Hence, a visual acuity of 20/20 may not be present in children below this age. Visual acuity should be tested in all children between the ages of 3–5 years. Vision testing at various ages is given in Table 4.49.

Visual field is tested by perimetry or confrontation method. Colour vision is tested by using Ishihara charts. Squint may be normally present up to 6 weeks of life. Presence of squint after this age should be evaluated. The squint can be paralytic or non-paralytic. In non-paralytic squint, visual defects may be present.

TABLE 4.49 Types of Visual Tests and Normal Visual Acuity at Various Ages

Age	Test	Visual Acuity
Newborn	Optokinetic nystagmus—eye movement is in the direction of black and white stripes	Visual acuity is 20/400
	Visual-evoked potential	Visual acuity is 20/100 to 20/200
Infancy	Responds to toys or familiar objects (like food items) of different sizes	Visual acuity is 20/100
1–2 years	Ability to follow rolling white balls of various sizes	Visual acuity is 20/50 to 20/100
2–3 years	A card is held in front of the baby. A similar card is held by the examiner and a letter is pointed out and the child is asked to show the similar letter in the card.	Visual acuity is 20/30 to 20/50
3–4 years	Modified or illiterate Snellen chart	Visual acuity is 20/50
Above 4 years	Can fixate its eyes on a coloured object	Visual acuity is 20/40
From the age of 5–6 years	Snellen chart	Visual acuity is 20/20

Visual Abnormalities. The following abnormalities in vision should be looked for in all children:

1. Refractive errors
   - Myopia—the rays are focused before the retina so that the vision for distant objects is defective.
   - Hypermetropia—the rays are focused behind the retina so that the vision for near objects is defective.
   - Anisometropia—the refractive power of the two eyes is different.
2. Amblyopia—this is also known as lazy eye. It is characterised by poor or indistinct vision in an eye which is otherwise normal physically, or poor vision which is out of proportion to the associated structural abnormalities. The transmission of the visual image to the visual cortex is poor or absent. This is usually seen in one eye. The development of normal vision requires that the visual cortex should receive focused images simultaneously from both the eyes. If this does not occur, the image from the dysfunctional eye is suppressed and amblyopia occurs. If the cause of this is not corrected, the image from the defective eye is permanently suppressed and leads to irreversible loss of vision in that eye. *Hysterical amblyopia* may be associated with constricted visual fields. Sometimes in hysterical amblyopia, the vision may be tubular and constricted, but the objective examination of the eye is normal. Amblyopia occurs in the following conditions:
   - Congenital cataract
   - Strabismus
   - Anisometropia due to significant difference in the refractive error of both eyes
3. Cortical blindness—the lesion in the visual cortex can lead to loss of vision in the presence of a normal pupillary reflex.
4. Nystagmus is abnormal when it is sustained. The nystagmus can be lateral, vertical or rotatory.

It is commonly seen in children with visual defects.

5. Vertical or skew deviation is seen in children with periventricular haemorrhage.
6. Metamorphopsia or distorted visual perception of an object's size, shape or position is seen in a condition known as 'Alice in Wonderland syndrome'. The defect in vision results in distorted image which is usually due to defect in retina. It may be seen in partial seizures, after hallucinogenic drugs, acute febrile illness and schizophrenia. The following distorted visual perceptions are seen.
   - Size of the image—micropsia is a condition where the objects perceived by the eyes are smaller than normal. Macropsia is a condition where the objects perceived by the eyes are larger than normal.
   - Position of the image—teleopsia is a condition when the object appears to be present at a distance away from where it is actually present.
   - Shape of the image may be distorted. For instance, a straight line may appear like a wave.
   - Hallucinations of figures or scenes—formed hallucinations are seen in temporal lobe lesions. Unformed hallucinations are seen in occipital lobe, anterior visual pathway or retinal lesions.

Clinical Approach. In a child presenting with visual impairment, the following high-risk factors should be checked:

- H/o infections and meningitis
- H/o head injury
- H/o infections like rubella (may cause cataract)
- H/o low birth weight, birth asphyxia and oxygen administration during birth
- H/o delay in social smile and other milestones
- H/o antimalarial drug intake
- Family history of visual problems

Look for external eye abnormalities, visual abnormalities and abnormalities of head and face during examination of a child with impaired vision. Microcephaly may be present in rubella.

MENTAL RETARDATION

A child is said to be mentally retarded when he cannot perform more than 2 standard deviations below the mean for his age on a standard psychometric test measuring intelligence. Mental retardation is common in children. It is important to diagnose and treat it at an early stage. Mild mental retardation may be missed. Many conditions resulting in mental retardation are either preventable or treatable. It is important to remove any offending agent which predisposes to mental retardation.

A child with mental retardation has the following characteristics:

- IQ below 70
- Impairment of adaptive behaviour—these children may have delayed milestones
- Onset before the age of 18 years

EARLY INDICATORS

A child should be evaluated for mental retardation if any of the following features are seen:

1. Abnormal facies/microcephaly
2. Altered sleep pattern—sleeps excessively
3. Short attention span, poor concentration, easy distractibility
4. Poor associative memory
5. Behaviour and emotional problems—emotional lability, explosive outbursts, temper tantrums, physically aggressive behaviour, self-mutilation, impulsiveness, bruxism
6. Clumsy movements, drowsiness
7. Hyperactivity, aimless overactivity
8. Delayed milestones
9. Neuropsychological developmental delay, abnormal intellectual functions, poor school performance and learning difficulties
10. Feeding difficulties—does not demand feeds, difficulty in sucking
11. Grading of intelligence—low
12. Persistent neonatal reflexes
    - Hand regard persists beyond 24 weeks of life (babies aged 12–20 weeks watch their hands)

- Mouthing (taking things to mouth) beyond 12 months of life
- Casting—throwing things on the floor usually stops by 15–16 months; it may persist beyond this age in mentally retarded children

13. Juvenile delinquency

HISTORY TAKING

Age

It is important to know the correct age of the child. Knowledge about what a normal child can perform at that age is necessary. Incorrect age may result in falsely labelling a child as mentally retarded. The tests used to assess intelligence are age-dependent.

Sex

Certain milestones are more advanced in a particular gender. The speech development is usually advanced in females. Certain conditions associated with mental retardation may be gender specific (Klinefelter's syndrome).

Place

A child from a rural background with no access to school facilities will perform less as compared to a child from urban area.

Presenting Complaints

- Poor school performance

History of Present Illness

- Developmental delay in speech or hearing
- Behavioural or psychiatric problems
- Learning problems
- H/o constipation (hypothyroidism)
- H/o intolerance to cold (hypothyroidism)
- H/o fire-setting behaviour (Klinefelter's syndrome)
- H/o unexplained seizures in early infancy—metabolic disorders
- H/o episodic vomiting (metabolic disorders)
- H/o PICA (lead poisoning)
- H/o dermatitis in the exposed parts (niacin deficiency causing pellagra)
- H/o involuntary movements (Wilson's disease)
- H/o self-mutilation
- H/o rage attacks
- H/o choreoathetosis
- H/o progressive weakness—mitochondrial myopathy, encephalopathy, lactic acidosis and stroke (MELAS) syndrome is a progressive neurodegenerative disorder
- H/o symptoms of autonomic dysfunction
- H/o deep metallic voice (William's syndrome)
- H/o excessive shyness or aggressiveness (Klinefelter's syndrome)
- H/o bony deformities at the elbow leading to restricted supination and flexion (Klinefelter's syndrome)
- In adolescents and adults, Klinefelter's syndrome should be ruled out if an adolescent presents with failure of development of secondary sexual characters, infertility and lack of libido

History of Past Illness

- H/o convulsions, altered sensorium (infections of CNS followed by postmeningitic sequelae, postencephalitic sequelae)
- H/o head injury

Antenatal History

- Age of mother at conception—advanced maternal age is associated with increased risk for Down's syndrome
- H/o miscarriages (intrauterine infections, genetic disorders)
- H/o decreased intrauterine movements (hypothyroidism, spinomuscular atrophy)
- H/o maternal hypothyroidism (cretinism)
- H/o maternal malnutrition (IUGR)
- H/o intrauterine infections—rubella, toxoplasmosis, cytomegalovirus, etc.
- H/o systemic diseases such as hypertension, heart disease, renal disease, toxaemia of pregnancy
- H/o teratogenic agents
- H/o antepartum haemorrhage

- H/o irradiation
- H/o multiple pregnancy
- H/o breech presentation—increases the chances of difficult labour and leads to increased chances of hypoxia, obstructed labour and birth injuries

Birth History

- H/o obstructed or prolonged labour
- H/o birth asphyxia—APGAR score at 5 minutes and delayed cry
- H/o birth injury
- H/o convulsions (hypoxic ischaemic encephalopathy and intracerebral haemorrhage)
- H/o low birth weight
- H/o prematurity

Neonatal History

- H/o jaundice
- H/o convulsions
- H/o feeding problems
- H/o sepsis

Growth and Development History

- H/o delayed motor and mental milestones
- H/o delayed development of speech and language
- H/o delayed psychomotor development
- H/o delayed scholastic performance
- H/o delayed puberty (Klinefelter's syndrome)

Nutritional History

The child may have history suggestive of malnutrition with nutritional myopathy in iodine deficiency disorders.

Personal History

This includes the child's dietary habits, sleeping habits and his relationship with other children. It is usually asked if the child is above 7 years.

History of Allergy and Contact

- H/o allergy—skin, nasal, respiratory and gastrointestinal allergies should be enquired. Any allergy to food or drugs should be enquired.
- H/o contact with a known case of tuberculosis—tuberculoma or chronic infection with tuberculosis will result in decreased school performance.

Family History

- H/o mental retardation—mental deficiency can be familial
- H/o consanguinity
- H/o low birth weight in siblings
- Intelligence of the parents

Environmental History

Poor sanitation facilities predispose to recurrent infections and infestations, vitamin deficiency and malnutrition which will predispose to mental retardation.

Socioeconomic History

Mental retardation is more common in low income groups. This is because the following factors which predispose to mental retardation are more common in low socioeconomic class:

- Maternal drug abuse like alcohol
- Infection rate
- Lack of time for caring and teaching children
- Lack of stimulation is also associated with mental retardation

GENERAL EXAMINATION

Rule out Klinefelter's syndrome in a tall adolescent who presents with failure of development of secondary sexual characters, gynaecomastia, hypogonadism, infertility, lack of libido or genital abnormalities (small phallus, small testes, testicular atrophy, hypospadias). Also look for attention deficit, hyperacusis (autism, William's syndrome) and hyperventilation (William's syndrome) in any child suspected to be mentally retarded. Head-to-toe examination of a mentally retarded child is given in Table 4.50.

Anthropometry

- Weight—decreased in foetal alcohol syndrome and malnutrition.

TABLE 4.50 Examination of a Child with Mental Retardation

Features	Clinical Examination and Significance	
Stature	Short stature	Mucopolysaccharidoses, hypothyroidism, bird-headed dwarf, other genetic disorders, etc.
	Tall stature	Genetic disorders
Dysmorphic facies	Cretinoid	Hypothyroidism
	Mongoloid	Down's syndrome
	Elfin facies	William's syndrome
Head	Microcephaly	Primary—Down's syndrome, Cri-du-chat syndrome, Cornelia de Lange syndrome, etc. Secondary—TORCH infection, hypothyroidism, etc.
	Macrocephaly	Neurodegenerative disorders (Alexander's disease, Canavan's disease, GM2 gangliosidosis, Tay–Sach's disease) Hydrocephalus, Subdural effusion Mucopolysaccharidoses
Hair	Double whorl Sparse hair, flag sign	Malnutrition
	Fine hair	Homocystinuria, hypothyroidism
Cheeks	Malar flush	Homocystinuria
	Prominent maxilla, baggy cheeks	William's syndrome
Eyes	Hypertelorism (widely set eyes)	Down's syndrome, William's syndrome
	Hypotelorism	Foetal alcohol syndrome
	Mongoloid slant	Down's syndrome
	Antimongoloid slant	Treacher–Collins Syndrome
	Microphthalmia	Congenital rubella syndrome
	Corneal ulcers	Familial dysautonomia
	Cataracts	Galactosaemia
	Cloudy cornea	Mucopolysaccharidoses, Lowe's syndrome
Fundus	Cherry-red spot	GM1 gangliosidosis, mucolipidosis, Niemann–Pick disease, Tay–Sachs disease
	Retinitis pigmentosa	Ataxia telangiectasia

(Table continued)

TABLE 4.50 *(Continued)*

Features	Clinical Examination and Significance	
Ears	Low set ears	Down's syndrome
Eyebrows	Synophrys	Cornelia de Lange syndrome Cretinism
Jaws	Small hypoplastic mandible	William's syndrome
Nose	Blunt upturned nose	William's syndrome
	Depressed nasal bridge	Down's syndrome
Teeth	Delayed dentition	Hypothyroidism
Palate	High arched palate	Down's syndrome
Neck	Short	Down's syndrome
Hands	Clinodactyly	Down's syndrome
	Micromelia	Cornelia de Lange syndrome
	Dermatoglyphics—increased 'atd' angle	Down's syndrome
	Single simian crease	Down's syndrome
Chest	Gynaecomastia	Klinefelter's syndrome
Joints	Stiff joints	Mucopolysaccharidoses
Abdomen	Hepatosplenomegaly	Mucopolysaccharidoses
Genitalia	Micropenis	Klinefelter's syndrome
	Ambiguous genitalia	45,X (Turner's syndrome and variants) 47,XXY (Klinefelter's syndrome and variants) Congenital adrenal hyperplasia
Skin	Photosensitivity	Hartnup disease
	Dermatitis	Phenylketonuria
	Acrodermatitis enteropathica	Zinc deficiency
Neurocutaneous markers	Café-au-lait spots	Ataxia telangiectasia, Bloom syndrome, neurofibromatosis, tuberous sclerosis
	Depigmented nevi	Tuberous sclerosis
	Adenoma sebaceum	Tuberous sclerosis

- Height—short stature in Down's syndrome, hypothyroidism, Laurence–Moon–Biedl syndrome; tall stature in Klinefelter's syndrome.
- MAC—decreased in severe malnutrition.
- Head circumference—decreased/increased.
- Upper segment/lower segment ratio—decreased due to long legs (Klinefelter's syndrome).

EVALUATION

Levels of mental retardation are assessed by measuring the developmental quotient or IQ.

1. Developmental quotient

$$\frac{\text{Developmental age}}{\text{Chronological age}} \times 100$$

For interpretation, see Table 4.51.

2. Intelligence quotient

$$\frac{\text{Mental age}}{\text{Chronological age}} \times 100$$

Intelligence quotient measures several functions of brain-like auditory, memory, visual–spatial compatibility and expressive and receptive language.

Developmental Scales

Various developmental scales are used to test the intelligence of a child. These are as follows:

1. Screening tests
   - Denver Developmental Screening Test
   - Phatak's Baroda Screening Test
   - Goodenough–Harris drawing test
2. Definitive tests
   - Bayley Scale of Infant Development
   - Stanford–Binet Intelligence Scale
   - Wechsler Intelligence Scale for Children

TABLE 4.51 Interpretation of Development Quotient

Developmental Quotient	Interpretation
≥85	Normal
71–84	Mild-to-moderate delay
≤70	Severe delay

Maximum score is usually 100. If the infant was born prematurely, the chronological age should be corrected for gestational age in the first year of life.

TABLE 4.52 Grading of Intelligence Quotient

Grading of IQ	Intelligence Quotient
Genius	>140
Super intelligent	120–140
Intelligent	110–119
Normal	90–109
Dullness	80–89
Borderline deficiency in intelligence	70–79
Feeble-mindedness	Under 70

TABLE 4.53 Tests for Intelligence

Test	Method	Age Group
Stanford–Binet Intelligence Scale (one of the best and most widely used)	Verbal ability, perceptional skills, short-term memory, hand–eye coordination.	2 years to adulthood
Binet–Kamat test	Indian adaptation of Stanford–Binet Intelligence Scale. It uses both verbal and performance tests.	3–22 years
Wechsler Intelligence Scale for Children	Verbal and performance scale.	5–15 years
Malin Intelligence Scale for Indian Children	Indian adaptation of Wechsler Intelligence Scale for children.	5–15 years
Goodenough Draw-a-Man Test	Ask the child to draw a man.	3–10 years

Intelligence Quotient

Intelligence quotient testing should be done when the child is not hungry or suffering from any illness. For grading of IQ, see Table 4.52. Tests for intelligence are given in Table 4.53.

GRADING

An IQ below 70 is considered as 'mental retardation' or limited mental ability. Five per cent of the population falls below 70 on IQ tests. Grading of mental retardation on the basis of IQ is given in Tables 4.54 and 4.55.

Mild Mental Retardation

Approximately 85% of the mentally retarded population is in the mildly retarded category. The cases often remain

TABLE 4.54 Grades of Mental Retardation

Grading of Mental Retardation	Intelligence Quotient
Mild mental retardation	51–69
Moderate mental retardation	36–50
Severe mental retardation	20–35
Profound mental retardation	< 20

TABLE 4.55 Alternative Grading System of Mental Retardation

Grading of Mental Retardation	Intelligence Quotient
Moron	50–70
Imbecile	25–49
Idiot	< 25

undiagnosed till late childhood. Their IQ score ranges between 51 and 69. They can often acquire academic skills up to the sixth grade level. They can become fairly self-sufficient and in some cases live independently, with community and social support.

Moderate Mental Retardation

About 10% of the mentally retarded population is considered moderately retarded. Moderately retarded individuals have IQ scores ranging between 36 and 50. They can carry out work and self-care tasks with moderate supervision. They typically acquire communication skills in childhood and are able to live and function successfully within the community in a supervised environment like a group home.

Severe Mental Retardation

About 3%–4% of the mentally retarded population is severely retarded. Severely retarded individuals have IQ scores of 20–35. They may master very basic self-care skills and some communication skills. Many severely retarded individuals are able to live in a group home.

Profound Mental Retardation

Only 1%–2% of the mentally retarded population is classified as profoundly retarded. Profoundly retarded individuals have IQ scores below 20. They may be able to develop basic self-care and communication skills with appropriate support and training. Their retardation is often caused by an accompanying neurological disorder. They need a high level of structure and supervision.

CATEGORISATION OF A MENTALLY RETARDED CHILD

According to the intelligence of the child, the mentally retarded child may be

- educable—can be put in special schools;
- trainable—can be trained for personal needs like eating, or vocational training for jobs which do not need much skill; or
- custodial—cannot be trained and needs care by a caretaker.

CAUSES

The causes of mental retardation can be present in the prenatal, natal or postnatal period.

1. Prenatal causes
   (a) Familial/genetic disorders
      - Chromosomal disorders—Down's syndrome, Klinefelter's syndrome, Carpenter syndrome, Cornelia de Lange syndrome, Coffin–Lowry syndrome, Coffin–Siris syndrome, bird-headed dwarfism (Seckel's syndrome), fragile X syndrome, incontinentia pigmenti, Klippel–Feil syndrome, Laurence–Moon–Biedl syndrome, Marshall–Smith–Lawrence syndrome, Prader–Willi syndrome, Rubinstein–Taybi syndrome, Sjogren–Larson syndrome, Sotos' syndrome, Smith–Lemli–Opitz syndrome, William's syndrome, etc.
      - Neurocutaneous disorders—tuberous sclerosis, neurofibromatosis
      - Metabolic disorders—summarised in Table 4.56
      - Storage disorders—mucopolysaccharidosis

   (b) Maternal factors
      - Intrauterine infections—rubella, toxoplasmosis, cytomegalovirus, HIV
      - Maternal malnutrition

TABLE 4.56 Abnormalities of Metabolism Causing Mental Retardation

Abnormalities in Metabolism	Disorders
Amino acid	Phenylketonuria Homocystinaemia Histidinaemia Hartnup disease Maple syrup urine disease
Carbohydrate	Galactosaemia
Lipid	Gaucher's disease Niemann–Pick disease

- Placental dysfunction/insufficiency
- Toxaemia of pregnancy
- Teratogenic agents
- Antepartum haemorrhage
- Irradiation

(c) Foetal factors

- Cerebral malformations
- Developmental defects (microcephaly, craniostenosis)

2. Natal causes
   - Birth asphyxia leading to hypoxic ischaemic encephalopathy
   - Birth injury
   - Intracerebral haemorrhage
3. Postnatal causes
   - Infections—meningitis, encephalitis
   - Hypoxia, asphyxia
   - Metabolic—hypoglycaemia
   - Nutritional deficiencies—malnutrition, vitamin deficiencies
   - Toxins—lead poisoning
   - Trauma—head injury, intracranial haemorrhage
   - Endocrine disorders—hypothyroidism
   - Electrolyte imbalance—hypernatraemia
   - Kernicterus
   - Cerebral palsy
   - Deafness
   - Postvaccine encephalopathies
   - Degenerative disorders—progressive encephalopathies (Gaucher's disease, leukodystrophies), subacute sclerosing panencephalitis (SSPE)
4. Other causes
   - Social causes—improper feeding of female child, child abuse
   - Cultural causes—delayed first feed of baby

DIFFERENTIAL DIAGNOSIS

- Motor deficits
- Speech defects
- Hearing defects
- Visual defects
- Psychiatric disorders

INVESTIGATIONS

1. Blood
   - Serum ammonia increased (N-acetylglutamate [NAG] synthetase deficiency, carbamyl phosphate synthetase [CPS] deficiency)
   - Serum lead increased (lead poisoning)
   - Serum zinc decreased (zinc deficiency)
   - Serum copper and ceruloplasmin increased (Wilson's disease)
   - Serum uric acid increased (Lesch–Nyhan syndrome)
   - Serum very long chain fatty acids increased (adrenoleukodystrophy)
   - Thyroid function studies (hypothyroidism)
   - Blood enzyme assays for metabolic disorders/hormonal studies for chromosomal disorders like Klinefelter's syndrome
   - Blood glucose (decreased in glycogen storage disorders)
   - Serological tests for intrauterine infections
   - Serum lactate and pyruvate increased (mitochondrial myopathy)
   - Serum calcium increased in William's syndrome
   - Markers of intrauterine infection
   - Viral titres for congenital infections
2. Urine
   - Screening tests for metabolic disorders—ferric chloride test (phenylketonuria), dinitrophenylhydrazine test (maple syrup urine disease), cyanide nitroprusside test (homocystinuria), Toluidine blue test (mucopolysaccharidoses)

- Reducing substances
- Urine chromatography

3. Radiological
   - X-ray skull may show calcifications—diffuse calcification is seen in toxoplasmosis, periventricular calcification is seen in cytomegalovirus infections, calcification in subdural haemorrhage, tram-track sign in Sturge–Weber syndrome
   - Ultrasonogram—hydrocephalus
   - CT scan—intracranial space occupying lesions, cerebral cortical lesions, tubers in tuberous sclerosis, dilated ventricles and cortical atrophy, porencephaly, absence of corpus callosum, hydrocephalus
   - MRI scan for degenerative disorders
4. Tissue biopsy for storage disorders
   - Testicular biopsy—small testes with hyalinised somniferous tubules, arrest of spermatogenesis, predominance of Sertoli cells (Klinefelter's syndrome)
5. Karyotyping
   - Chromosomal disorders like Down's syndrome, Klinefelter's syndrome
6. EEG (electroencephalogram)
7. Prenatal Diagnosis
   - Triple test (β-hCG, estriol and α-fetoprotein) for Down's syndrome
   - Amniocentesis
   - Ultrasound—nuchal thickness scan
   - Chorionic villus sampling

TREATMENT

1. Medical
   - Thyroxine replacement for hypothyroidism
   - Diet therapy in children with phenylketonuria and galactosaemia
   - Treatment of Klinefelter's syndrome—replacement therapy with long-acting testosterone should be started by 11–12 years of age
2. Surgical
   - Early surgical intervention for craniostenosis and congenital hydrocephalus
3. Supportive care
   - Special education for mentally retarded
   - Institutional care for severely retarded

PREVENTION

Some cases of mental retardation can be prevented by early intervention. Hence, a high index of suspicion is needed for early evaluation and management in such children. Conditions associated with preventable causes of mental retardation are as follows:

1. Perinatal factors
   - Birth asphyxia—improved perinatal care
   - Intrauterine infections—screening and treatment
   - Maternal malnutrition—dietary management
2. Metabolic disorders
   - Phenylketonuria—early diagnosis and dietary management
   - Galactosaemia—early diagnosis and dietary management
   - Gaucher's disease—genetic counselling
3. Endocrine disorders
   - Hypothyroidism—antenatal screening, early screening of newborn and treatment
4. Nutritional disorders
   - Malnutrition—dietary management
   - Prevent nutritional deficiencies
5. Infections
   - Congenital rubella syndrome—immunisation of girls
6. Miscellaneous
   - Hydrocephalus—early diagnosis and treatment
   - Kernicterus—early diagnosis and treatment of neonatal jaundice
   - Avoid teratogenic drugs like antithyroid drugs in pregnancy
   - Avoid alcohol drug abuse, tobacco irradiation during pregnancy
   - Genetic counselling
   - Family support

PREDISPOSING FACTORS

In any child with mental retardation the conditions that should be ruled out or treated are given below.

Causes of fall in mentation	
A	Abuse (physical or sexual) of the child
B	Bad child rearing practices
C	Cerebral cortex lesions—infarction, haemorrhage Cultural factors
D	Drug addiction Degenerative disorders like Niemann–Pick disease Drugs—pseudodementia due to drugs
E	Emotional deprivation
F	Fits—epilepsy Familial factors
G	Glucose decreased—hypoglycaemia Galactosaemia
H	Hydrocephalus Hypernatraemia Hearing defects
I	Injury—head injury Infections of CNS—meningitis, encephalitis
J	Juvenile hypothyroidism
K	Korsakoff psychosis due to niacin deficiency Kernicterus due to hyperbilirubinaemia
L	Lead poisoning Learning disorders Late onset storage disorders
M	Malnutrition Metabolic disorders—phenylketonuria, aminoaciduria Mucopolysaccharidoses Motor neuron disease
N	Niemann–Pick disease
O	Ocular problems—visual problems, loss of vision
P	Psychotic problems Personality disorders
Q	Quotient—intelligence decreased
R	Receptive aphasia Retinal/visual defects
S	SSPE (subacute sclerosing panencephalitis)
T	Tumours in the CNS Teratogenic effect of drugs and alcohol, foetal alcohol syndrome
U	Unexplained causes
V	Vitamin niacin deficiency—dementia (pellagra) Visual defects
W	Wernicke's encephalopathy Wilson's disease—copper metabolism abnormal

FUTURE DEVELOPMENT OF RETARDED CHILDREN

Most parents are anxious about the future development of their child. This, however, cannot be predicted. Hence, one should refrain from giving assurance about the future intelligence or school performance of the child. The future development depends on the following factors:

- Illness
- Injury
- Social factors like parental care
- Nutrition of the child
- Environmental factors
- Stimulation of the child
- Opportunities provided to the child

The developmentally retarded children cannot compete with the normal children. Hence, it is important to support them in various fields like educational opportunities and job placements. The child's capabilities can be assessed and the work can be allotted accordingly. For example, certain jobs which do not require intelligence like buttoning the shirts can be allotted to them. Interestingly, in the state of Tamilnadu a separate board was formed by the government in the year 2010 to take care of the developmentally retarded people and provide support to them in the form of job opportunities.

DYSLEXIA

Dyslexia is reading difficulty due to defective cortical processing of graphic symbols. There is difficulty in learning to read despite adequate intelligence and sociocultural opportunity. This can be primary or secondary to brain injury, hormonal influences or developmental defects.

- Primary dyslexia is due to dysfunction of the cerebral cortex on the dominant side, usually the left side, and does not change with age. It is hereditary and can run in families. It is more common in boys than girls. These children have difficulty in reading, writing and spelling. They also have difficulty in processing information from seeing, hearing and participating in activities.
- Secondary dyslexia or developmental dyslexia due to hormonal changes occurs during early stages of foetal development. It is common in boys and diminishes as the child matures.
- Trauma dyslexia is due to trauma or injury to the brain which controls reading and writing.

Dyslexia may be visual or auditory:

- Visual dyslexia—number and letter reversals and inability to write symbols in the correct sequence.
- Auditory dyslexia—difficulty in perceiving sounds.

CLINICAL FEATURES

The following features depend on the age of the child and severity of the disorder:

- Right–left disorientation
- Letter reversal and mirror writing
- Difficulty in rhyming words
- Learns words slowly
- Delay in speech
- Low letter knowledge—difficulty in learning alphabets in order
- Difficulty in identifying or generating rhyming words or counting syllables
- Difficulty in word retrieval
- Difficulty in learning to decode words
- Difficulty in distinguishing between similar sounds in words
- Difficulty in reading, slow inaccurate reading
- Difficulty in organisation skills
- Difficulty in comprehension of instruction given rapidly or following more than one command at a time
- Difficulty in remembering sequence of things
- Writing of sentences containing similar words with unrelated meaning, for example, cat/rat, sweet/sweat

ASSOCIATED COMORBIDITIES

- Dysgraphia—ability to hold and control the pencil or pen while writing.
- Dyspraxia—knowing the orders of words to be written but writing in a wrong order.
- Dyscalculia—difficulty in learning fundamentals of one or more basic numeric skills.
- Developmental dyspraxia—difficulty in carrying out routine tasks.
- Cluttering—a speech fluency disorder. The rate and rhythm is affected which results in impaired speech intelligibility.

DIFFERENTIAL DIAGNOSIS

Dyslexia should be differentiated from other conditions which cause problems in reading such as the following:

- Acquired word blindness (alexia) due to lesion in the dominant cerebral hemisphere
- Brain disease (organic damage)
- Cultural deprivation
- Dietary factors—malnutritional delay
- Educational deprivation
- Emotional disturbances
- Sensory defects
- Intellectual impairment

CHAPTER 5

Nutritional Disorders

Nutritional problems are common in children. These include improper diet habits, overfeeding and underfeeding. Parents and paediatricians should be aware of the dietary needs of various age groups and the early features of the nutritional deficiencies.

HISTORY TAKING

The important aspects of history and examination in children with suspected nutritional disorders are given below.

Name

The name may give a clue about the number of children in the family or the birth order without directly asking for it. For instance,

- Aruchamy: sixth child
- Panchalingam: fifth child
- Ezhumalai: seventh child
- Ettappan: eighth child

When the total number of family members increases, the risk for malnutrition becomes more.

Age

Different nutritional disorders are prevalent at different ages in children. The age of the child may help the clinician to diagnose the type of nutritional disorder he/she is suffering from. For example, marasmus is more common in infancy and kwashiorkor in the age group of 1–4 years.

Sex

Malnutrition is common in female children as they are neglected in most families, particularly in the lower socioeconomic group. They are neglected because the parents feel that the girls will go to some other house after marriage. This gender bias, although abhorrent, leads to preferential nurturing of the male child both in terms of education and nutrition.

Place

The place of origin and current residence can alert the examiner to look for certain nutritional disorders. Children from places where healthcare facilities are poor or not available, as in certain tribal areas, are prone to suffer from malnutrition. The topographic location of the place may predispose the child to certain nutritional deficiencies. For example, iodine deficiency is common in hilly areas. Historical events that alter the lifestyle significantly may also affect the nutritional status. For instance, children from drought-hit areas or areas affected by natural calamities and wars, such as Ethiopia and Sri Lanka, are prone to develop malnutrition.

Informant

Informant may be the mother or other caretakers. Many malnourished children come from home for destitutes. In such cases, history should be obtained from both the mother and the guardian taking care of the child.

Reliability

The reliability of the informant should be assessed before using the history procured from him/her to diagnose the condition. For example, history obtained from the mother is more reliable than that from a caretaker or a distant relative not living with the child. If the caretaker is not giving proper care to the child, the information given by him/her may not be reliable.

Presenting Complaints

The presenting complaints relevant to the nutritional status should be recorded in the chronological order of their appearance. The examiner should record the presenting complaints in the informant's/patient's own words and avoid asking any leading questions at this stage. Some examples of presenting complaints relevant to nutritional status include 'child is not gaining weight' and 'child has repeated loose stools'.

History of Present Illness

History of present illness includes the details of the presenting complaints in the order of appearance. Box 5.1 contains some common points that the examiner should enquire about when eliciting the history of present illness for nutritional disorders. The examiner should make detailed enquiry about each presenting complaint by asking leading questions (Table 5.1). Medical terminologies such as diarrhoea and dyspnoea can be used to describe the history. Table 5.2 enlists some important points that could alert the examiner to look for vitamin deficiencies.

BOX 5.1 History of present illness

Oedema (hypoproteinaemia)
Vomiting
Diarrhoea
Abdominal distension (muscle hypotonia due to hypocalcaemia, ascites due to hypoproteinaemia)
Failure to thrive
Ear discharge (CSOM)
Skin lesions (exanthem)
Recurrent respiratory tract infection (more than six episodes every year)
Chronic renal failure (oliguria, polyuria) and persistent urinary tract infections (burning micturition, haematuria) are associated with loss of appetite and malnutrition
Jaundice (liver disorders are associated with loss of appetite)
Steatorrhoea (malabsorption)
Pica (ingestion of inedible things like mud or pencil commonly seen in children with iron deficiency anaemia, worm infestation or mental retardation)
Wasting of muscles (due to utilisation of muscle proteins)
Decreased activity (child is dull and not interested in the surroundings)
Feeding difficulties (seen in children with cleft palate)
Swallowing problems (seen in children with cerebral palsy)
Loss of appetite
Loss of weight (due to utilisation of body stores)
Dyspnoea, chest pain, palpitations (congestive cardiac failure in wet beriberi due to thiamine deficiency, kwashiorkor)

Past History

Past history is very important in children with malnutrition. Events like infections, fever and diarrhoea precipitate malnutrition (Table 5.3). Previous history of hospitalisation and surgery should be taken. Surgical resection of part of gut leads to malabsorption of certain nutrients.

TABLE 5.1 Leading Questions to Elicit H/o Oedema, Vomiting and Diarrhoea

Presenting Condition	Leading Questions
Oedema	Which region was involved first? (e.g. legs, face)
	What was the mode of onset?
	How did it evolve?
	Is the oedema progressive or non-progressive?
Vomiting	How did it start? What was the onset like?
	How many episodes of vomiting has the child suffered from?
	What was the nature of vomiting? (e.g. projectile)
	What were the contents of the vomitus?
	What was the time interval between the last feed and the vomiting?
	Did the child pass any worms in the vomitus?
Diarrhoea	Onset—How did it start?
	Duration—How long has the child been having loose stools?
	Frequency—How many times does the child pass stool in a day?
	Consistency—Is it watery or mucoid?
	Volume—Does the child pass normal, less or large amount of stool?
	What is the colour of the stool passed?
	Is it foul-smelling, blood stained, frothy or oily?
	Does the child pass mucous or worms along with stools?
	Is it precipitated by particular type of food?
	Is it accompanied by vomiting or abdominal pain?
	Has the child been given any laxative?
	What are the factors that decrease the diarrhoea (including details of treatment)?
	What was the usual diet given to the child during the episode?
	Was it associated with any mass descending per rectum? (rectal prolapse is common in patients with diarrhoea.)

Treatment History

Prolonged treatment may be due to chronic infections which lead to malnutrition. Prolonged drug therapy may lead to malabsorption of certain nutrients.

TABLE 5.2 Vitamin Deficiency and Relevant History

Deficient Vitamin	History to Ask About
Vitamin A	Poor dark adaptation Night blindness Photophobia (due to xerosis or corneal ulcer)
Vitamin K	Bleeding tendency Muscle weakness (myopathy)
Vitamin B_{12}	Difficulty in walking (neuropathy)
Vitamin D	Bony deformities

TABLE 5.3 Relevance of Past History

Past History	Relevance
Exanthematous fever	Past history of measles is usually associated with malnutrition. Measles induces immunosuppression and predisposes the child to secondary infection.
Tuberculosis	Tuberculosis is usually associated with loss of appetite. It persists for a long duration.
Whooping cough	Whooping cough makes the posterior pharynx so sensitive that intake of food generally induces vomiting. This predisposes to malnutrition. For fear of vomiting the child avoids eating.
Diarrhoea	It results in decreased transit time which decreases the time of contact of the food and intestinal absorptive surface. Also, many mothers withhold certain food items during diarrhoea which further predisposes to malnutrition.
Jaundice (chronic liver disease)	It is associated with loss of appetite.

For example, treatment with isoniazid predisposes to pyridoxine deficiency. Children with chronic inflammatory diseases respond poorly to drugs and are often associated with malnutrition.

History of Contact

The examiner should enquire about any prolonged contact of the child with anyone suffering from communicable diseases such as tuberculosis.

Antenatal History

The antenatal events are important because the potential for growth depends upon the number of

TABLE 5.4 Relevance of Antenatal History

Antenatal History	Relevance
Age of the mother	Young primi mothers are not mature enough to give birth to a child. Elderly mothers develop complications which may affect the foetus.
Weight of the mother	Maternal malnutrition predisposes to low-birth-weight babies.
Immunisation	Immunisation of the mother prevents certain diseases such as rubella in the mother. These intrauterine infections also affect the foetus.
National programme beneficiary	If the mother has been benefited by various national programmes and has received adequate nutritional supplementation during pregnancy, the child is less likely to have nutritional deficiencies perinatally. Usually 100 tablets of iron and folic acid are given during pregnancy.
Antenatal check-up (regular/irregular)	Regular antenatal check-up is needed to correct any nutritional deficiencies in the mother. They are given proper advice regarding diet, prevention of infections, sleep, rest, hygiene, etc.
Weight gain during pregnancy	The normal weight gain during pregnancy should be 10 kg.
Work profile during pregnancy	Working mothers are more prone to nutritional deficiency.
Time period since previous pregnancy	Usually an interval of more than 24 months is recommended between two consecutive pregnancies.
H/o hypertension or diabetes	These predispose to placental insufficiency.
H/o urinary tract infection	This may result in premature delivery.
H/o threatened abortion or sepsis	This predisposes to placental insufficiency.
H/o maternal malnutrition (e.g. anaemia)	If maternal iron stores are low, the foetus is likely to suffer from anaemia.

cells. Any factor which decreases the nutrient supply to the growing foetus has a negative effect on the postnatal period (Table 5.4).

Birth History

Birth history refers to the events during the delivery of the child. Any complication like birth asphyxia or meconium aspiration affects normal feeding of the baby. If the baby is born at home or in some remote rural area, where medical facilities are not available, the baby may have been fed with prelacteal feeds. Also, breastfeeding may be withheld if the mother had any problem like fever or diarrhoea. A primi mother may not be aware of the proper feeding techniques (Table 5.5).

TABLE 5.5 Relevance of Birth History

Birth History	Relevance
Birth order (first, second or third baby)	The babies born later are prone to malnutrition especially when the interval between two successive pregnancies is less than 2 years. The nutritional stores in the mother may be insufficient. Sometimes, the previously born baby may be neglected as the care is diverted to the newborn child.
Gestational age (preterm/term/postterm)	Preterm babies have low birth weight and poor sucking reflex. Postterm babies may be affected due to placental insufficiency.
Birth weight	Low-birth-weight babies may not be able to feed well. This predisposes to malnutrition.

Postnatal History

The following should be taken care of during history taking:

- Inability to suck (preterm, HIE hypoxic ischaemic encephalopathy)
- Infections (septicaemia, bronchopneumonia)
- Bad child rearing practices–instillation of oil in the nose
- H/o diarrhoea
- Any other illness needing separation from mother
- Congenital defects
- Cardiac defects associated with failure
- Rooming in (baby and mother placed together)–early or delayed
- Feeding—breastfed or bottle-fed
- Weight gain—adequate or not (should gain 30 g/day for first 3 months)

BOX 5.2 Leading questions to elicit postnatal history

- What was the time interval between birth and the first feed?
- What was the first feed given to the baby?
- Was it colostrum or some other prelacteal feed?
- If the first feed was not colostrum, what was given to the baby?
- When was colostrum given to the baby in case the first feed was prelacteal?
- Was the baby hospitalised?
- Why was the baby hospitalised and for how long?
- Are there any records of the events that took place during the hospitalisation?
- Was the weight gain monitored or not?

Some leading questions to elicit postnatal history are given in Box 5.2.

Developmental History

The developmental milestones should be enquired in detail. Both mental and motor milestones are delayed in children with severe malnutrition. The following points should be asked while noting the developmental history:

- Are the milestones acquired normal/delayed for age?
- Is there any loss in the acquired milestones?
- Is there any deterioration in school performance? This may be due to malnutrition.

Pellagra due to niacin deficiency may present with mental retardation and dementia. Thiamine deficiency affects both mental and motor development. Hypocalcaemic rickets is associated with delayed motor milestones due to hypotonia.

Diet History

The diet history includes the details of the food intake of the child right from birth to the present day. The examiner should enquire about the feeding during neonatal period, early and late infancy and in childhood (Table 5.6). Feeding pattern is important since the newborn period. Breastfeeding starting soon after birth protects from diseases like obesity in later life. A detailed nutritional history is of value in diagnosis and management of the child.

Special focus should be given to the diet immediately before the nutritional disorder. This can be done by creating a diet chart that contains the details of the diet taken by the child in 1 day (Table 5.7). The clinician should also calculate the total calories and proteins in the food consumed.

TABLE 5.6 Leading Questions to Elicit Diet History

Period	Leading Questions
Neonatal period	When breastfeeding was started after the birth?
	Did the child receive colostrum?
	Did the child get any prelacteal feed? If yes, what?
	Was the child on exclusive breastfeeding? If not, then what did the additional feeding consist of?
Infancy	When was complementary feeding started? Complementary food is defined as non-breast milk foods or nutritive liquids given to young children to complement the breastfeeding. Complementary feeding should be started at about 6 months of age.
	What did it consist of? (cow's milk/formula feeds/ any other)
	Was it given whole or diluted? If diluted, what was the dilution?
	How was it given? (by bottle/paladai/any other)
	How long was breastfeeding continued?
Older children	Is the diet predominantly vegetarian or non-vegetarian?
	What is the kind of food usually taken? (to assess the quantity and quality of diet)
	Has the child ever been a beneficiary of noon meal scheme?
Special conditions	Has the child ever been hospitalised? If yes, what was the diet during and after hospitalisation?
	What was the diet during diarrhoeal illness, if any?

TABLE 5.7 Sample Diet Chart to Record Food Intake in a Day

Time	Food Item	Quantity	Calorie Value	Protein Content
7.00 am				
9.00 am				
11.00 am				
1.00 pm				
4.00 pm				
8.00 pm				
Total				

Immunisation History

In the immunisation history, the clinician should record the various vaccines administered to the child. The age at which they were given should also be recorded. Refer to Table 2.11 for the prescribed immunisation schedule with timing, dosage and route of administration. If the child is not immunised, he/she is more prone to the following preventable diseases which affect the nutritional status of the child:

- Measles predisposes to malnutrition by decreasing the immunity and thereby increasing the incidence of infections, especially bronchopneumonia and gastroenteritis.
- In pertussis, the posterior part of the pharynx becomes sensitive. Even a slight stimulus at this part precipitates cough and vomiting. Hence, the child avoids eating. Even if the child eats, he/she tends to vomit.
- Tuberculosis is a chronic infection which is associated with loss of appetite and thereby predisposes to malnutrition.

All infections result in loss of appetite (decreased intake) and increased metabolism; hence, they predispose to malnutrition.

Personal History

The food habits and the type of foods consumed affect the child's health. Nowadays, most children prefer junk foods which do not give calories and proteins in required proportions. A detailed personal history should be taken to bring out any factor which predisposes to malnutrition. Some sample questions to elicit personal history are given in Box 5.3.

BOX 5.3 sample questions to elicit personal history for nutritional disorders

- What are the food habits of the child?
- Does the child have any food fads?
- Does he/she have any strong likes and dislikes for any particular food item?

History of Allergy

Children may not tolerate certain foods. They may develop allergic reactions like rashes and itching.

Food allergy is abnormal response to food. There is exaggerated susceptibility to certain food items. For instance, allergy to sea foods or cow's milk may manifest as asthma, abdominal pain, anaphylaxis, urticaria, angioneurotic oedema, etc.

Intolerance to food items is present when a child is not able to tolerate certain foods and presents with diarrhoea or vomiting. For instance, a child may not tolerate breast milk, cow's milk and egg due to protein intolerance.

Family History

The nutrition of the child depends upon the number of family members, food habits in the family and the attitude of the parents towards their children. Hence, a detailed family history should be taken (Table 5.8).

Certain malabsorptive disorders may run in families. If a genetic cause is suspected, a family pedigree should be drawn.

Socioeconomic History

Malnutrition is more common in low socioeconomic class. Obesity and related complications are common in upper socioeconomic class (Box 5.4).

PHYSICAL EXAMINATION

In a child suspected to have any nutritional disorder, the examiner should do a complete head-to-toe examination, including examination of all the systems.

TABLE 5.8 Leading Questions to Elicit Family History Relevant to Malnutrition

Family History	Leading Questions
Consanguinity	Is marriage within close relatives permissible? Does the marriage of the child's parents fall in this category?
Number of siblings	How many brothers and sisters does the child have?
Birth order	How many of them are older and how many younger to the child?
Illness	Do any of the family members currently residing with the child suffer from any communicable disease? Has any hereditary condition been present in the family similar to that in the child?
Family fads	Is there any custom/culture that the family follows with respect to nutrition? (e.g. fasting, vegetarian diet, excess fried food, etc.)
Miscellaneous factors	Is the mother pregnant again? (breastfeeding compromised) Do both the parents stay with and care for the child?

General Examination

A careful systematic head-to-toe examination gives a lot of clue to the cause and type of nutritional deficiency. It helps the clinician to look for all the signs of nutritional disorders. Table 5.9 includes the typical findings seen in various nutritional disorders during the head-to-toe examination.

Vital Signs

The vital signs should be monitored carefully. Change in vital signs often gives a clue to the development of complications which need urgent intervention.

- Heart rate—increased in cardiac failure due to thiamine deficiency.
- Respiratory rate—increased in metabolic acidosis due to starvation.
- Temperature—increased in presence of infections. In severe malnutrition, the temperature may not increase in presence of infections or it may be even decreased in many cases. Children with malnutrition, especially kwashiorkor, are prone to hypothermia which should be either prevented or identified early and treated.

BOX 5.4 Leading questions to elicit socioeconomic history

- How much is the average income of the family? (to assess per capita income)
- How much of it, on an average, is spent on food products?
- What is the literacy status and educational background of parents?
- What do the parents do for a living?
- How many hours does the mother spend away from the child because of her work?
- What is the location of the house?
- How is the neighbourhood?
- Is the house thatched or pukka?
- How many rooms are there in the house?
- What is the average size of the rooms? (to assess living space)
- How many doors and windows does the house have? (to assess the adequacy of ventilation)
- What is the source of drinking water?
- Is the water boiled/filtered/treated in any other way before consumption?
- Does the family have sanitary toilet facilities?
- How many toilets are there and how far are they placed from the source of drinking water?
- How far is the house located from the nearest medical facility?

- Blood pressure—decreased in severe malnutrition. In wet beriberi, the blood pressure may be decreased due to cardiac failure.

Anthropometry

Anthropometry is the study of the measurements of the human body. This gives an early clue to nutritional disorders. In acute malnutrition, there is weight loss only. In chronic malnutrition, both weight and height are less than expected for that particular age. The following body measurements are usually done to assess the nutritional status of the child.

- Weight
- Height or length
- Head circumference
- Chest Circumference

TABLE 5.9 General Examination of a Child with Nutritional Disorder

Examination	Observation
Consciousness (sensorium)	Normal Altered (lethargic, drowsy, obtunded, stuporous, comatose)
Nutritional status	Well nourished Malnourished (marasmic, undernourished, overweight, obese) Generalised wasting
Mental state	Alert or dull
Emotional state	Happy, comfortable and interested in surroundings Resents examination, ill, irritable, peevish, apathetic, not interested in the surroundings
Oedema	Generalised oedema (anasarca) Pedal oedema
Nails, conjunctiva and lymph nodes	Pallor, cyanosis, icterus, clubbing, lymphadenopathy
Head-to-toe examination	
Head	Shape (Caput quadratum in rickets) Size (microcephaly in chronic malnutrition) Anterior and posterior fontanels (closure delayed in malnutrition, rickets) Bossing (in rickets) Craniotabes (softening of outer table of skull in rickets)
Hair	Hypopigmented, sparse, thin, easily pluckable, brittle, lustreless (malnutrition) Alopecia (zinc deficiency, kwashiorkor) Flag sign (altered bands of normal and hypopigmented hair in kwashiorkor)
Face	Moon face (in kwashiorkor) Old man appearance (in marasmus)
Eyes	Conjunctival xerosis, Bitot's spots, corneal xerosis/ulcer (in vitamin A deficiency) Pallor (in anaemia) Puffy eye lids (in hypoproteinaemia)
Ears	Ear discharge (in chronic suppurative otitis media [CSOM] which is commonly associated with malnutrition)
Mouth	Angular stomatitis, cheilitis (in vitamin B deficiency) Oral thrush, caries teeth, pharyngitis, tonsillitis Noma—ulcer on the cheek due to infection caused by fusospirochetosis which may perforate the cheeks. It is known as cancrum oris Cleft lip/cleft palate (decreases intake and predisposes to malnutrition)

(Table continued)

TABLE 5.9 *(Continued)*

Examination	Observation
Tongue	Glossitis, magenta red tongue (riboflavin deficiency) Bald tongue (in vitamin B_{12} deficiency) Beefy red tongue (in niacin deficiency)
Gums	Bleeding gums seen in vitamin C deficiency
Teeth	Delayed dentition (vitamin D deficiency) Pulp defects (phosphate deficiency) Enamel defects (in calcium deficiency)
Neck	Lymphadenopathy (tuberculosis may be associated with malnutrition)
Chest	Rachitic rosary (vitamin D deficiency) Scorbutic rosary (vitamin C deficiency) Harrison's sulcus (vitamin D deficiency)
Abdomen	Distension due to loss of muscle tone (in hypokalaemia)
Rectum and anus	Perianal excoriation (in lactose malabsorption, chronic diarrhoea) Rectal prolapse (in chronic diarrhoea)
Extremities	Oedema (due to hypoproteinaemia) Wasting (muscle wasting in marasmus and kwashiorkor) Skin lesions—skin changes of kwashiorkor, dermatitis in niacin deficiency Phrynoderma in vitamin A or essential fatty acid deficiency Bony deformities in rickets (widening of wrists, genu varum, genu valgum, genu recurvatum, double malleoli)
Nails	White nails (in hypoalbuminaemia) Brittle nails (in iron deficiency anaemia) Nail deformities (spoon-shaped nails) Transverse ridges on nails due to interrupted growth
Skin	Pallor (in anaemia) Dermatosis (paddy field, flaky paint in kwashiorkor) Distribution of skin lesions (symmetrical/asymmetrical in secondary infections) Dermatitis in the areas exposed to sunlight (seen in niacin deficiency) Decreased skin turgor (in marasmus) Impetiginous lesions (infections of skin due to immunodeficiency) Hypopigmentation/hyperpigmentation (both are seen in kwashiorkor; hyperpigmented areas denude to form hypopigmented patches) Flexural ulcers, bullous lesions (in kwashiorkor) Erythematous macules, well marginated with large dark brown scales (dermatitis of areas exposed to sunlight like face, arms and feet in pellagra—deficiency of nicotinic acid) Phrynoderma (asymptomatic hard, follicular papules; results in toad-like skin; seen in vitamin A and essential fatty acid deficiency) Petechiae, poor wound healing (in vitamin C deficiency)

- Midarm circumference (MAC)
- Skinfold thickness
- Weight for height (expected weight for present height)

Decrease in weight is followed by decrease in skinfold thickness, MAC, chest circumference, height and head circumference in that order.

Systemic Examination

Nutrient deficiencies can affect any part of the body. For example, thiamine deficiency presents with cardiac failure in wet beriberi and neurological symptoms in dry beriberi. Hence, a thorough examination of all the systems is important to recognise and treat complications at an early stage. Also, the system affected gives a clue to the type of deficiency. For instance, musculoskeletal system is affected in vitamin D deficiency, while coagulation system is affected in vitamin K deficiency.

Gastrointestinal System

Important findings in abdominal examination are as follows:

- Free fluid in peritoneal cavity due to hypoproteinaemia
- Organomegaly—hepatomegaly in kwashiorkor
- Distension of abdomen (pot belly) due to hypotonia of anterior abdominal wall muscles (hypocalcaemia)
- Paralytic ileus, abdominal distension (hypokalaemia)

Respiratory System

Respiratory infections are common in vitamin A deficiency. Important findings in examination of respiratory system include

- dyspnoea, tachypnoea (bronchopneumonia, pyothorax predispose to malnutrition) and
- tachypnoea due to acidosis in severe malnutrition.

Cardiovascular System

Wet beriberi due to thiamine deficiency presents with cardiac failure. Dilated cardiomyopathy is common in selenium deficiency (Keshan's disease). Important findings in examination of cardiovascular system include the following:

- Haemic murmurs in anaemia. The haemic murmurs are systolic murmurs heard due to hyperdynamic circulation which causes increased flow in the normal valves. Hyperdynamic circulation occurs as a compensatory measure in anaemia
- Cardiomegaly (cardiac failure as in kwashiorkor)
- Tachycardia due to congestive cardiac failure (as in kwashiorkor)
- Absent heart sounds in pericardial effusion due to hypoproteinaemia

Central Nervous System

Important findings in examination of central nervous system include the following:

- Apathy/dullness (marasmus)
- Irritability is seen in kwashiorkor
- Wernicke's encephalopathy
- Korsakoff's psychosis
- Dementia and mental retardation are seen in niacin deficiency
- Subacute combined degeneration is seen in vitamin B_{12} deficiency
- Hypotonia due to decreased potassium and calcium.
- Decreased power due to niacin deficiency and hypocalcaemia
- Diminished reflexes in pyridoxine deficiency

The clinical findings seen in various nutritional disorders are summarised in Table 5.10.

FEEDING OF AN INFANT

An infant should be exclusively breastfed till 6 months of age. Exclusive breastfeeding means that no additional food or fluid (including water) should be given to the infant. After 6 months of age, complementary feeding is introduced and it is given in addition to the breastfeeding. Complementary food is defined as non-breast milk foods or nutritive liquids given to infants to complement the breastfeeding. This is important as the infant's increasing nutritional requirements cannot be met

TABLE 5.10 Summary of Clinical Findings in Various Nutritional Disorders

Nutritional Disorder	Clinical Findings
Marasmus	Hypopigmented hair Loose folds of skin Dry, scaly and inelastic skin
Kwashiorkor	Skin oedema Flaky paint/crazy pavement/paddy field dermatosis Hypopigmentation/hyperpigmentation Flexural ulcers Purpura/ecchymosis/easy bruisability Bullous lesions Thin, sparse, dry and easily pluckable hair
Vitamin A deficiency	Scaly skin Phrynoderma (toad-like skin) Xerophthalmia
Thiamine deficiency	Polyneuritis
Riboflavin deficiency	Glossitis Cheilosis Nasolabial dyssebacea Peripheral neuropathy
Niacin deficiency	Pigmented, scaly and cracked skin on parts exposed to sun
Biotin deficiency	Peripheral neuropathy
Vitamin C deficiency	Maculosquamous dermatitis Scurvy Bleeding gums
Vitamin D deficiency	Short stature Skull—frontal bossing, craniotabes, delayed fontanel closure Teeth—delayed dentition, enamel defects, pulp defects Chest—rosary, Harrison sulcus Hands—widening of wrists Legs—genu varum, double malleoli
Vitamin E deficiency	Myopathy Neuropathy
Vitamin K deficiency	Bleeding
Copper deficiency	Hypopigmented hair and skin
Zinc deficiency	Alopecia Acral dermatitis Acrodermatitis enteropathica)
Essential fatty acids deficiency	Phrynoderma (toad-like skin)

by breastfeeds alone after this age. Different flavours and variety of nutritional foods are introduced in the child's diet at appropriate ages. Some of these are given in Table 5.11.

TABLE 5.11 Feeding of an Infant

Age	Nutritional Food
Birth to 6 months	Exclusive breastfeeding
From 6 months onwards	Breast milk Complementary feeds
7–8 months	Curds can be added
9 months	Egg yolk can be added
10–11 months	Egg white can be given
12 months	Can share the parent's food without spices; takes 4–5 meals a day

BREASTFEEDING

Breastfeeding provides all the nutrients that a baby needs, as well as those substances that promote growth and fight infection. In fact, for the first 6 months of life, the baby does not require any food other than breast milk. Under normal circumstances, even extra water is not needed during this period (Table 5.12).

Preparation of the breast tissue for breastfeeding starts well before the birth of the baby. Hormonal changes in the female body during pregnancy prepare the breast to produce milk. After birth, when the baby first sucks the mother's breast, the nerves in the areola stimulate the pituitary gland to release the hormones prolactin and oxytocin. Prolactin makes the lobules (the milk-producing tissues in the breast) secrete milk. Oxytocin makes the smooth muscles surrounding the lobules squeeze the milk into the breast's ductal

TABLE 5.12 Types of Breastfeeding

Types	Intake
Exclusive breastfeeding	Only breast milk; nothing else, not even water
Predominant breastfeeding	Apart from breastfeeds, small amount of other foods or fluids like water
Partial breastfeeding	Some breastfeeds and some artificial feeds
Token breastfeeding	Mostly other foods, occasionally breastfeeds

system. This response is known as *let-down* or *milk ejection reflex*. The ductal system then carries the milk to the nipple where the baby suckles.

Types of Breast Milk

The milk secreted at the beginning of a feeding session is called *foremilk*. This is different in composition than the hind milk or later milk, which is the milk secreted towards the end of the feeding session. Foremilk contains more of proteins, vitamins, minerals, water and sugar and quenches baby's thirst; whereas hind milk is much richer in fats, provides more energy, satisfies baby's hunger and nutritional demands. Both these portions of breast milk are necessary for the optimal growth and development of the baby. The baby should therefore be allowed to empty one breast before being offered the other breast.

The composition of breast milk also varies, depending on the needs and requirements of the baby. The milk secreted when the baby is 2–3 days old is different from that secreted when the baby is 10 days or older. Additionally, the milk of a mother who has delivered a preterm baby is different from that of a mother who has delivered a full-term baby. The varying composition of breast milk is tabulated in Table 5.13. The proportion of nutrients in mature breast milk is given in Table 5.14.

Frequency of Feeds

A newborn infant normally feeds at least 8–12 times a day during first few weeks. Number of feeds per day varies according to the age of the baby.

- Initially every 1–4 hours as per demand (demand feeding)
- 6–9 feeds by first week of life
- 3–5 meals by 9–12 months of age

The amount of milk secreted in the first 2 days is 30–50 mL only. However, with continued

TABLE 5.13 Varying Composition of Breast Milk

Type	Time	Appearance	Composition	Function
Colostrum	First 3–4 days after birth	Yellowish and thick	More antibodies and white blood cells Anti-infective agents (lactoferrin, lysozyme, lactoperoxidase, complements, proline-rich polypeptides) Rich in vitamins A, D, E and K Less fats More proteins and immunoglobulins (IgA, IgG, IgM) Rich in growth factors (like epidermal growth factor, fibroblast growth factor)	Protection against infection Has a mild laxative effect; helps to pass early stools
Transitional milk	4 days to 10–14 days	Thinner, lighter in colour	More fat, sugar, calories and vitamins Less immunoglobulin and protein.	Supplies adequate calories needed by the baby
Mature milk	2 weeks after the baby is delivered	Thinner	More fat, protein, water, lactose, energy (71 cal/100 mL) Less minerals Growth factors and protective agents	Supplies all nutrients needed for normal growth
Preterm milk	When a preterm baby is delivered		More calories, fat, proteins, sodium, immunoglobulin and lactoferrin Zinc, macrophages Less lactose, calcium and phosphorus	Supplies more energy which is needed for rapid growth
Foremilk	At the start of feed	Watery	Rich in proteins, sugar, vitamins, minerals and water	Satisfies baby's thirst
Hind milk	At the end of feed	Thick	Richer in fat content	Provides energy, satisfies baby's hunger and nutritional demands

TABLE 5.14 Proportion of Nutrients in Mature Breast Milk

Category	Component	Content/100 mL
Macronutrients	Calories	71 kcal
	Carbohydrates	7 g
	Proteins	1.1 g
	Fat	3.8–4.2 g
	Lactose	7.0 g
Micronutrients (minerals and trace elements)	Sodium	0.9 mEq/L
	Potassium	1.4 mEq/L
	Calcium	34 mg
	Phosphorus	15 mg
	Iron	0.05–0.1 mg/L Bioavailability is 49%
	Zinc	120 µg
Vitamins	Vitamin A	170–670 IU
	Vitamin C	5.2–10 mg
	Vitamin D	0.5–10 IU
	Vitamin E	0.56 µg
	Vitamin K	1.5 µg
Water	88%	Adequate to excrete the solutes by the kidneys
Protective substances	Immunoglobulins (IgA and IgM) Leucocytes Macrophages and lymphocytes Bifidus factor Lactoferrin Lysozyme Para-aminobenzoic acid	Present
Miscellaneous	Lactalbumin, whey protein, taurine, essential fatty acids	Rich content

breastfeeding, the milk production increases to up to a maximum of 700 mL per day by 5–6 months.

How to Feed the Baby

The baby should be breastfed on demand rather than by an hourly schedule. During feeding, the baby should be allowed to feed from one breast until the milk flow stops spontaneously. Then the mother should offer the other breast, allowing the baby to feed until completely satisfied. Halting feedings after a predetermined time may prevent the infant from obtaining the extra fat and calories in the hind milk necessary for proper growth.

Guidelines for positioning and attachment of the baby during breastfeeding

Proper positioning

- The infant's head, neck and body should be held in a straight line.
- The whole of the baby's body should be supported, not just the head and neck.
- The baby's face should be directly in front of mother's breast (en face).
- The baby's body should be close to the mother's body.

Proper attachment

- The chin should touch the breast.
- The mouth of the baby should be wide open.
- The baby's lower lip should be turned out.
- Most areola and nipple should be in baby's mouth. More areola should be visible above than below the baby's mouth.

Proper positioning and attachment of the baby during breastfeeding are illustrated in Figs. 5.1 and 5.2.

Adequacy of Breast Milk

Under usual circumstances, for a baby younger than 6 months, the amount of breast milk secreted is enough for the baby's nutrition and development. Even malnourished mothers have adequate milk supply for their babies; however, the content of IgA, proteins and lipids may be lower in such milk.

In case, the mother feels that her feeds are not enough for her baby, she should be advised to carry out the wetness test (Box 5.5). The wetness test is a simple, time-honored technique for mothers with perceived milk insufficiency to overcome their anxiety and avoid top-up supplements. It is based on the baby's urine output. If the baby passes six to eight times urine per day, it implies that the baby is getting enough milk. If the baby passes concentrated



FIGURE 5.1 Proper positioning of the baby during breastfeeding.

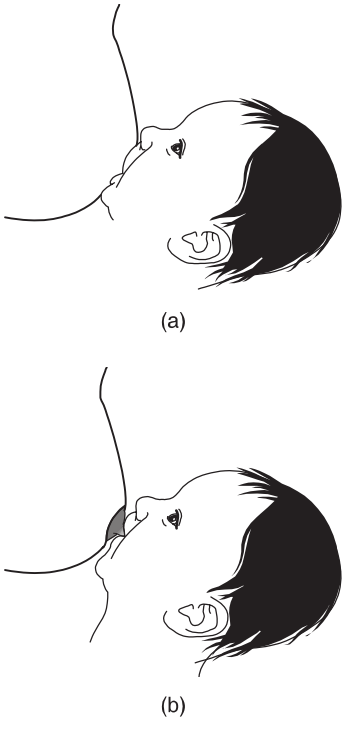


FIGURE 5.2 Breastfeeding. (a) Good attachment. (b) Poor attachment.

urine less than 6 times per day, it implies that he/she is not getting enough milk. Hence, wetness test is a simple test which provides objective evidence to the mother that the baby is getting adequate feeds.

Another simple way to assess the adequacy of the breast milk is to regularly weigh the child. For the first 7 days, the baby usually loses weight. It starts gaining weight after 7 days, and by the 10th day, the weight is equal to its birth weight. After 10th day, normal full-term babies have a daily weight gain of 30 g for the first 3 months.

Additionally, after a full feed, the baby is satisfied and demands another feed approximately 2–3 hours later. Adequately breastfed babies pass several golden-yellow stools per day. Some signs to identify actual breastfeed insufficiency are enumerated in Box 5.6.

BOX 5.5 The wetness test

Precondition
- Baby less than 6 months of age only on breast milk and no other fluids or feeds.

Observation
- The baby passes urine more than 6 times in 24 hours.
- The urine is clear, colourless and of good quantity.

Inference
- The baby is getting all the nutrition and fluid needed and there is no insufficiency.

BOX 5.6 How to identify that breast milk is not enough for the infant?

- Baby has inadequate weight gain or the weight remains stationary.
- The baby cries soon after feeding.
- The baby has constipation.
- The baby falls sick often.

Modes of Feeding

A nursing mother who is away from the baby for long durations (e.g. at work) can express and refrigerate the breast milk, which can be used to feed the baby later. In such a case, the expressed breast milk should be given to the baby by a paladai.

Tube feeding may be adopted for babies who are too ill to suckle or have a condition like cleft palate. The nasogastric tube used to feed a baby is usually of size 6–10 Fr. The length of the tube should be measured from the philtrum to the tragus and then from tragus to xiphisternum before inserting it. After insertion, the clinician should push air

BOX 5.7 Indicators of nasogastric tube being placed in the respiratory tract

- Tube placed under water shows bubbling of air
- Tube placed near a mirror fogs the mirror
- A feather or cotton placed at the mouth of the tube moves with each respiration

and auscultate over the stomach area to check its position. Box 5.7 enumerates some safety checks to ensure that the tube is not in the respiratory tract. The nasogastric tube should be changed every 24–48 hours. Tube feeding should be given in accordance to the stomach capacity. For instance, stomach capacity on first day is 10 mL/kg of body weight. Hence, a baby weighing 3 kg can be given about 30 mL tube feeds every 2 hourly.

Advantages of Breastfeeding

Breastfeeding is beneficial not just for the baby but also for the mother and family.

Advantages for the Baby

1. Nutritive value—breast milk contains all the nutrients that a baby needs for the first 6 months of life for optimal growth and development. It contains calcium and phosphorus in the ratio of 2:1, which protects against neonatal hypocalcaemia and infantile tetany. Breast milk contains water-soluble vitamin D along with a fat-soluble fraction. This protects the baby from rickets. It also contains more vitamins A, C and E than cow's milk (Table 5.15). The iron present in the breast milk is absorbed better than that in the cow's milk. Bioavailability of iron is more. About 50% of the iron from breast milk is absorbed.
2. Easily digestible—breast milk contains a higher proportion of whey proteins (lactalbumin and lactoglobulin) whereas cow's milk contains more casein (Tables 5.15 and 5.16). Whey proteins form finer curds and are more easily digested by the baby. Breast milk contains enzyme lipase. The active lipase in breast milk promotes digestion of fats and provides free fatty acids easily. Breast milk is also rich in oleic acid.
3. Kidney protection—breast milk has low sodium and mineral content. Also, the protein content of the breast milk is low. This decreases the solute load on the kidneys, which have low concentrating ability especially in the first week of life. The amount of lactalbumin is high. Lactalbumin is absorbed better by the neonatal kidney.
4. Brain development—taurine and cystine content of the breast milk is more. The amino acids in the breast milk are useful for brain development. The higher content of polyunsaturated fatty acids (PUFA) promotes brain growth. Breastfed children have higher intelligence quotient (IQ) as compared to those on artificial feeds.
5. Cardioprotective—the higher PUFA content in breast milk also protects the individual from atherosclerosis later in adult life.
6. Retinal development—long-chain PUFA present in the breast milk are helpful in retinal development.
7. pH of the breast milk is low. Hence, organisms do not grow in the breast milk. Also there is no risk of contamination.
8. Anti-infective factors—breastfed babies have fewer episodes of diarrhoea, respiratory and middle ear infections than top-fed babies. A baby who continues to breastfeed during an infection recovers more quickly than a baby who is denied breast milk. This is because the breast milk contains humoral and cellular anti-infective properties.
   - Humoral anti-infective factors—breast milk contains secretory IgA, IgM, lysozymes, C_3, C_4 and C_5 proactivators, antistaphylococcal factor and specific inhibitory substances (interferon) against viral infections.
   - Cellular anti-infective factors—colostrum has live phagocytic macrophages and lymphoid cells, which provide non-specific gastrointestinal host defenses and offer protection against diarrhoea and necrotising colitis (Table 5.17).
9. No risk of milk allergy—breast milk has a higher concentration of secretory IgA that inhibits the absorption of macromolecular protein. Cow's milk has a higher macromolecular protein

TABLE 5.15 Comparative Composition of Breast Milk and Cow's Milk

Components	Breast Milk	Cow's Milk
Calories/100 mL	71	67
Sugar (g/100 mL)	6.5–7	4.5–4.8
Total proteins (g/100 mL)	0.9–1.1	3.3–3.5
Casein (g/100 mL) 30%–40%	0.5	3.0 80%
Lactalbumin (g/100 mL)	0.7	0.5
Whey protein (lactalbumin and lactoglobulin) to casein ratio	Ideal ratio 60:40 Contains 60%–70% of whey protein (lactalbumin, lactoglobulin) and 30%–40% casein	Too high
Amino acids	Adequate for brain development	Inadequate for brain development
Fats	3.8–4.2 g/100 mL, polyunsaturated, required for brain growth and as a source of energy	3.6 g/100 mL, more saturated
Minerals (g/100 mL)	0.2	0.7
Iron (mg/L)	0.05–0.1 only, but bioavailability is 49%	0.05–1; however, bioavailability is less than 10%
Enzymes	Lipase present which helps digest fats in the presence of bile	Lacks adequate digestive enzymes
Lactose (g/100 mL) Aids brain development	7.5	4.5 Not present in adequate amount
Total salts	Required amount	Excess amount, results in increased load on kidneys
Sodium (mEq/L)	7	22
Chloride (mEq/L)	11	29

(Table continued)

TABLE 5.15 *(Continued)*

Components	Breast Milk	Cow's Milk
Potassium (mEq/L)	13	35
Calcium (mg/100 mL)	34	117
Phosphorus (mg/100 mL) Required amount	15	92 Excess amount, may lead to tetany
Calcium to phosphorus ratio Protects against neonatal hypocalcaemia	>2:1	<2:1 Predisposes to tetany
Total vitamins	Adequate Contains more of vitamins A and C	Not adequate
Vitamin A	53 µg 170–670 IU	34 µg 140–280 IU
Vitamin C (mg)	1.2–10.8	0.9–4
Vitamin D (µg)	1–1.8 0.5–10 IU	0.01–0.1 0.5–4 IU
Vitamin E (µg)	0.56	0.06
Vitamin K (µg)	1.5	6.0
Water Adequate to excrete the solute load by the kidneys; additional water not needed	88%	Same but inadequate to excrete the solutes by the kidneys; additional water needed to help kidneys excrete extra salts
Osmolality (mOsmol/kg)	290–300	Above 300
Renal solute load (mOsmol/L)	79	221
Protective substances	Immunoglobulins Leucocytes Bifidus factor *Lactobacillus bifidus* Lactoferrin Lysozyme Antibodies	Not present
Bacterial contamination	Less likely	More likely

TABLE 5.16 Differences in Digestion of Breast Milk and Cow's Milk

Characteristics	Breast Milk	Cow's Milk
Digestion	Easily digested and well absorbed	Not easily digested and well absorbed
Flocculation	Contains 60% whey proteins and 40% casein which forms small amount of floc-culent curd and finer precipitates, which are readily digested and absorbed	Contains 18% whey protein and 82% casein which forms large amount of casein curd, larger precipitates and are more difficult to digest
Fats	Remain unbound	Bound to casein
Gastric pH	Not affected	Increased (raised pH reduces pepsin activity)
Gastric emptying time	Shortened	Prolonged

content, which disrupts the immature intestinal mucosa of a 6- to 8-week infant. In the absence of secretory IgA, cow's milk protein acts as an antigen and may lead to allergy (Table 5.15). There is no risk of milk allergy in exclusively breastfed infants.

10. Protection from other allergies and diseases—breastfed babies have less chance of developing hypertension, obesity, coronary artery disease and diabetes in their adulthood. Breastfed babies are also protected against respiratory allergies, including asthma. The other diseases that are less common in breastfed babies include urinary tract infections, hypernatraemic dehydration, dental caries, neonatal convulsions and sudden infant death syndrome. Also, the incidences of diseases like inflammatory bowel disease, atherosclerosis, Hodgkin's lymphoma and sudden infant death syndrome are less even in later life.
11. Physiological adaptation—breast milk is not just species-specific but also individually tailored to the needs of the baby. A mother who has delivered prematurely secretes milk that is easily digested and is nutritive for her preterm baby. The low osmotic load in preterm milk is especially suited for premature infants. Even for a term baby, the composition of breast milk varies according to the age of the baby (colostrum, transitional and mature milk) as well as the phase of its feeding (fore- and hind milk).
12. Emotional bonding—breastfeeding promotes close physical and emotional bonding between the mother and the baby. This leads to better parent–child adjustment and fewer behavioural disorders in children.
13. Other benefits—the risk of overfeeding is minimal and the child has less tendency to develop vomiting. If the mother has been adequately immunised, breastfeeding also provides oral passive immunisation. Breast milk contains epidermal growth factor which promotes intestinal maturation.

TABLE 5.17 Humoral and Cellular Anti-Infective Factors in Breast Milk

Anti-infective Factor	Advantages
Humoral anti-infective factors	
Secretory IgA	Comprises 90% of the immuno-globulins in the human milk which protect the mucosa
Lactoferrin, transferrin	Iron-binding proteins inhibit growth of *Escherichia coli (E. coli)*
Bifidus factor	Promotes growth of *Lactobacillus bifidus* which decreases the pH of the intestines by metabolising lactose to lactic acid and acetic acid. This inhibits the growth of *E. coli* in the gut
Lysozymes	Enzymes with bacteriolytic action
Complements—C_3 and C_4	Opsonisation and chaemotactic action
Para-aminobenzoic acid (PABA)	Provides protection against malaria
Antistaphylococcal factor	Inhibits growth of staphylococci
Interferon	Antiviral factors
Cellular anti-infective factors	
Macrophages	Phagocytosis Synthesise lysozymes, lactoferrin, C_3 and C_4
Lymphoid cells	T cells transfer delayed hypersensi-tivity responses to the infant B lymphocytes synthesise IgA

Advantages for the Mother

1. Birth control—lactation suppresses ovulation. Mothers who breastfeed their infants regularly have lactational amenorrhoea and are at minimal risk of pregnancy at least for the first 6 months after delivery.
2. Maternal health—breastfeeding enhances involution of the uterus. It also lowers the risk of ovarian and breast cancer in the mother.
3. Convenience—this mode of feeding is more convenient for the mother as she is not required to clean the bottle and prepare the milk for artificial feeding several times during the day and night.

Economic Factors

1. Reduced food cost—even though the lactating mother needs additional food supplements, the cost of human milk is negligible as compared to the animal milk or commercially obtained powdered milk for artificial feeding. Cost of feeding bottles, rubber teats and fuel for preparation of alternative milk add significantly to the cost of artificial feeding.
2. Reduced healthcare cost—breastfeeding reduces healthcare costs by reducing illness among children, and so reduces the financial strain on the family and the nation.
3. Ecological benefits—breast milk is easily available at an optimal temperature and there is no wastage. It does not require fuel to be burnt and thus is ecofriendly.

Differences in Breast Milk and Cow's Milk

It is important to know the differences in composition and digestion of breast milk and cow's milk (Tables 5.15 and 5.16). Examination of stool also gives a clue to the consumption of breast milk or cow's milk (Table 5.18).

TABLE 5.18 Differences in Stools of Breast- and Cow's Milk-Fed Babies

Stool Characteristics	Breastfed Baby	Cow's Milk-Fed Baby
Consistency	Soft	Firm
pH	4–6	5–8
Flora	Predominately fermentative	Mixed flora
Odour	Fermentative	Putrefactive
Colour	Yellow-green	Yellow-brown
Number of stools/day	3–4	1–2

Steps to Promote Breastfeeding

1. Baby-friendly Hospital Initiative (BFHI)—BFHI was launched in 1992 by the WHO and UNICEF as part of the 'Innocenti Declaration' for promotion, protection and support of breastfeeding. Baby-friendly hospitals are required to adopt the breastfeeding policy and its 10 steps for successful implementation of breastfeeding practices. The initiative has been implemented in over 150 countries. The 10 steps to successful breastfeeding include the following:
   - Have a written breastfeeding policy that is routinely communicated to all healthcare staff.
   - Train all healthcare staff in skills necessary to implement this policy.
   - Inform all pregnant women about the benefits and management of breastfeeding.
   - Help mothers initiate breastfeeding within half an hour of birth.
   - Show mothers how to breastfeed, and how to maintain lactation even when they are separated from their infants.
   - Give newborn infants no food or drink other than breast milk, unless medically indicated.
   - Practice 'rooming-in'. Rooming-in policy allows mothers and infants to remain together throughout the day (all 24 hours).
   - Encourage mothers to breastfeed on demand.
   - Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding infants.
   - Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic.
2. The Infant Milk Substitutes, Feeding Bottles and Infant Foods (Regulation of Production, Supply and Distribution) Act 1992—the Government of

India has taken this step to protect and promote breastfeeding. This legislation prevents and prohibits advertising of infant milk substitutes and feeding bottles to the public. It also prohibits free sampling, hospital promotion and gifts or samples of infant milk substitutes and feeding bottles to the health workers. Violation of this act can lead to fine or imprisonment. The IMS Amendment Act 2003 strengthens the 1992 Act in the following ways:

- Prohibits labelling of infant foods.
- Prohibits the distribution of education materials.
- Funding of health workers and their organisations for better implementation and effective enforcement of the above act.

The main aim is to promote exclusive breastfeeding for the first 6 months and then to continue it up to 2 years of age.

Associated Problems and Contraindications

Despite all the benefits of breastfeeding, there are few problems which may be associated. These are enumerated in Table 5.19. It is advisable to avoid breastfeeding in certain conditions which may be maternal or related to the neonate.

1. Mother contraindications
   - Maternal psychosis
   - Maternal conditions like breast abscess, cracked nipple
   - Drugs like antimetabolites, antithyroid drugs, anticoagulants
2. Neonatal contraindications
   - Inborn errors of metabolism like phenylketonuria, galactosaemia and lactose intolerance
   - Hyperbilirubinaemia (rapidly increasing levels) due to breast milk jaundice

Special Circumstances

Feeding of the infant is modified in certain special circumstances.

TABLE 5.19 Few Problems Associated with Breastfeeding

Factors	Disadvantages
Amount of feeds taken	Not known
Infections	Cytomegalovirus, human immunodeficiency virus, hepatitis B from the infected mother
Drugs	Transmitted through milk are antithyroid drugs, antimetabolites, cathartics
Toxic substances	Nicotine, alcohol, caffeine
Breastfeeding jaundice	Seen in exclusively breastfed babies due to inadequate lactation in first 2 or 3 days of life. This predisposes to relative dehydration and haemoconcentration. Also, colonisation of bacteria in the gut is delayed; thereby conversion of bilirubin to stercobilin is delayed. This results in increased enterohepatic circulation
Breast milk jaundice	Self-limiting unconjugated hyperbilirubinaemia seen at the end of first week of life. This is due to presence of 3α, 20β-pregnanediol which inhibits hepatic conjugation of bilirubin
Vitamin K	Deficiency is common in breastfed babies; can present with haemorrhagic disease of newborn
Prolonged breastfeeding without complementary feeding	Protein energy malnutrition

Lactose Intolerance

- Primary lactose intolerance—lifelong lactose-free diets are given.
- Secondary lactose intolerance—temporary cessation of breastfeeding or lactose-containing feeds is done.

Feeding the Infant of an HIV-Positive Mother

Breastfeeding has a 15% risk for HIV transmission. An HIV-infected mother should be given the information on relative risks, advantages and disadvantages of particular feeding practice in a scientific and unbiased manner. This is called infant feeding counselling.

Feeding Options. The following four options should be given to the mother:

- Exclusive breastfeeding with early discontinuation of breastfeeds—the risk of transmission through the breast milk should be explained to the mother. But even after that if the mother is willing to breastfeed the baby, the baby can be breastfed. Exclusive breastfeeding is given for first 3 months. It is then stopped abruptly and changed to tinned foods. This reduces the risk of the baby getting infected from the mother who is HIV positive. The duration of the exposure of the infant to the virus in breast milk will be reduced, thereby reducing the risk.
- Modified breastfeeding—breast milk may be heat-treated by pasteurisation. The milk is heated to 62.5°C for 30 minutes and then allowed to cool. After heat-treating, it should be used within 1 hour.
- Breastfeeding from an HIV-negative woman (wet nursing)—feeding the infant of an HIV-positive mother by another HIV-negative woman is called wet nursing. The mother and the wet nurse should be counselled for breastfeeding. The mother should accept the fact that the baby will be fed by a wet nurse. The following points should be explained to the wet nurse. She should be told about the risk of contracting the infection from the infected baby. She should feed the baby for 6 months and should not discontinue in between. She should be available to feed the baby when required. She should follow safe sexual practices, which prevents her from acquiring infection during the breastfeeding period.
- Total replacement feeding from birth—the baby is not given breast milk right from birth.

Prelacteal Feeds

Prelacteal feeds are artificial feeds or drinks given to a baby before breastfeeding is initiated. The prelacteal feeds are dangerous because of the following reasons:

- The babies are more likely to develop infections such as diarrhoea, septicaemia and meningitis.
- Babies are more likely to develop intolerance to the proteins in the artificial feeds and allergies such as eczema.
- They interfere with suckling.
- The baby's hunger is satisfied, so it accepts less breast milk.
- Sucking confusion, or nipple confusion—if the babies are fed from a bottle with an artificial teat, they may have more difficulty attaching to the breast.
- The baby suckles less, resulting in less stimulation of the breast.
- Breast milk takes longer to come in and it is more difficult to establish breastfeeding. If a baby receives even few prelacteal feeds, his/her mother is likely to suffer from breast conditions such as engorgement. Bottle feeding is likely to suppress the production of breast milk.

Complementary Feeding

The maximum amount of breast milk secreted in a day is usually not more than 700 mL, which supplies about 500 calories. When the calorific requirement of the baby exceeds 500 calories a day (usually by 6 months of age), extra nutritional intake is required. This extra food in addition to the breast milk is called *complementary feeding*. Weaning means stopping breast milk to start solid food whereas complementary feeding implies adding extra nutrition to continued breastfeeds. Hence, it is preferable to use the term complementary feeding instead of weaning.

Even after complementary feeding is started, breastfeeding should continue for at least the first year of life and possibly into the second and third years for optimal development of the child. Beyond that age, mother's milk should be increasingly supplemented with solid food and other fluids. Breastfeeding may be continued for as long as the baby feeds from breast or till the secretion of breast milk stops. There is no hard and fast rule that it has to be stopped by 2 years..

How to Start

The changeover from breast milk to other foods should be done gradually. This gives both the mother and the child the time for biochemical and psychological adjustments. Abrupt cessation of breastfeeding can lead to potential complications in the mother, for example breast engorgement. Sudden

introduction of the complementary diet added with abrupt stoppage of breastfeeding can lead to frequent gastrointestinal upsets in the baby.

Complementary feeding should be started with clear fluids. Then a gradual change in the consistency of diet can be done from liquid to semisolid and then to solid foods. Foods of thicker consistency should be introduced one at a time with a gap of 1 week between new foods. Initial feeds may include thin gruel of rice or porridge, mashed potatoes or green vegetables. Curds can be added by 7–8 months of age.

The complementary food should be given before the breastfeeds when the child is hungry. It should be started with small quantity of one to two teaspoon initially and the quantity can be increased gradually. The baby should never be forced to eat.

A new food should be started only when the child gets adapted to the previous item introduced. It is prudent to observe the child for food allergy every time a new food is introduced.

During the introduction of semisolid food, the baby often tends to spit the food out. This is because the tongue movement for drinking is very different from that for eating and the baby has to learn this technique. Spitting out at this stage may not be a sign of allergy or intolerance.

The food should always be freshly prepared in clean utensils (preferably home-cooked). It should be palatable, acceptable, affordable, available and free from contamination.

After 7–8 months of age, most infants like to hold and eat their food. They can be given biscuits, crackers, bread, potatoes and chicken, liver or minced chicken to eat. Eggs, meat and fish are usually introduced during the latter half of the infancy to avoid chances of allergy. Egg yolk can be added by 9 months. The egg white should be started later by 10–11 months of age as it has a greater potential of creating food allergy.

By 8–9 months of age, infants can hold their feeding bottle and try to drink directly from a cup. A 10-month-old infant usually tries to eat with a spoon. By their first birthday, most infants are able to share table food (without spices) and take four to five meals a day. At 1 year of age, a baby should be at least three times its birth weight and eat almost half as much as its mother does.

Normal babies, who are breastfed and then weaned off to balanced and nutritious home-made foods at the right time, do not require any special supplements of vitamins and minerals.

For older infants who can accept the same foods as consumed by the parents, provide basic four items in the diet. Daily food should contain the following four groups of food:

1. Milk/curd
2. Cereals/pulses group
3. Vegetables (green leafy vegetables)/fruits
4. Meat/egg

NUTRIENTS

Nutrients are constituents in the food which should be supplied in adequate amounts for optimal growth.

CLASSIFICATION

I. On the basis of requirement

1. *Macronutrients:* These are needed in large amounts by the body
   - Carbohydrates
   - Proteins
   - Fats
2. *Micronutrients:* These are needed in small quantities, often less than 100 mg
   - Vitamins
   - Minerals: These are further classified into macrominerals and trace elements. Macrominerals are present in high concentration in the body more than 0.01% body weight (i.e., more than 0.1 mg/g or 100 µg/g) and are needed in relatively large quantities as compared to trace elements. Trace elements are present in concentration less than 0.01% body weight (i.e., less than 0.1 mg/g or 100 µg/g) and are needed in small quantities, often less than 100 µg/day

II. On the basis of function

1. *Energy-yielding foods:* Carbohydrates and fats
2. *Bodybuilding foods:* Proteins
3. *Protective foods:* Vitamins and minerals

4. *Regulatory foods:* Water and roughage (dietary fibres)

NUTRIENT INTAKE VALUES

This refers to the recommendations on dietary substrate for healthy people to maintain the state of normal health and development. Nutrient intake values (NIV) are based on physiological requirements and are important for the following reasons:

- To assess intake
- To provide guidance for appropriate food intake
- To provide food-based dietary guidelines
- To serve as basis for nutrition policies and nutrition education programmes
- To provide reference points for labelling food products

DAILY REQUIREMENTS

Daily requirement of various nutrients depends upon the age, gender, weight and health conditions of the child. Recommended daily allowance (RDA) is the nutrient intake considered adequate to meet the known nutrient needs of practically all healthy children in a particular age. Energy requirement of a child is defined as the amount of energy needed to balance total energy expenditure. The energy requirement of a 1-year-old infant is 1000 kcal/day roughly. This requirement keeps on increasing with increase in age. Box 5.8 gives an approximate method for calculation of the energy requirement in children of various age groups. An alternative method for calculation based on weight is given in Table 5.20. Indian Council of Medical Research (ICMR) recommendations for calorie and protein requirements are given in Table 5.21.

BOX 5.8 Method for calculating calorie requirement per day

1000 kcal for 1 year
Add 100 kcal/year up to 12 years
For example, energy requirement of a 4-year-old child is 1000 + (100 × 3) = 1300 kcal

TABLE 5.20 Holliday–Segar Formula for Calculating the Daily Requirement of Calories

Weight of the Child (kg)	Daily Requirement of Calories (kcal//kg)
<10	100
10–20	1000 + 50
>20	1500 + 20

TABLE 5.21 Calorie and Protein Requirements of Children (ICMR Recommendations)

Age	Calories (kcal/kg/day)	Proteins (g/kg/day)
0–3 months	120	2.2
4–6 months	115	1.8
6–9 months	110	1.8
9–12 months	105	1.5
1 year	100	1.5
2–3 years	120	1.4
4–6 years	80–90	1.3
7–9 years	70–80	1.2
10–12 years	60–70	1.25

CARBOHYDRATES

Carbohydrates are the main source of energy and provide about 55% of the total calorie requirements. Based on the number of single carbohydrate units present, carbohydrates can be classified as monosaccharides, disaccharides or polysaccharides. The main categories of carbohydrates include

1. Energy-yielding carbohydrates
   - Monosaccharides—glucose, fructose, galactose. They cannot be hydrolysed into simple compounds
   - Disaccharides—lactose, maltose, sucrose
   - Polysaccharides—starch, dextrins, glycogen, pectin
2. Non-energy-yielding carbohydrates—dietary fibres

Advantages

Benefits of consuming adequate carbohydrates are as follows:

- It is a good source of energy.

- Protein sparing effect so that protein can be utilised for bodybuilding and repair.
- Regulation of fat metabolism—carbohydrates are necessary for normal oxidation of fats. In the absence of carbohydrates, fats are metabolised faster than in normal conditions.

Glycaemic Index

Glycaemic index describes the effect of carbohydrates on the blood glucose levels. A food with high glycaemic index will raise the blood glucose levels more rapidly than the one with low glycaemic index. Food with low glycaemic index causes small fluctuations in the blood glucose and insulin levels. glycaemic index is high for glucose and low for legumes. Carbohydrates with low glycaemic index are preferred for diabetic patients. Advantages of food with low glycaemic index.

- Reduces the risk for heart diseases
- Increases the sensitivity of the body to insulin
- Improves blood cholesterol levels
- Supplies glucose for a longer time; thereby helps prolong the physical endurance
- Reduces hunger
- Helps to lose weight

Dietary Fibres

Dietary fibres or non-starch polysaccharides constitute that part of the food which is not digested by the human digestive enzymes. These include cellulose (found in the plant cell walls) and chitin found in the fungi and mushroom. Although dietary fibres do not have any calorific value, they help in the process of digestion and assimilation (Box 5.9). The various types of dietary fibres are enumerated in Table 5.22.

TABLE 5.22 Types of Dietary Fibres

Type of Fibres	Examples
Fibrous forms	Cellulose Hemicellulose Lignins
Viscous forms	Pectins Gums

BOX 5.9 Importance of dietary fibres

- Add to the bulk of faeces and relieve constipation.
- Contribute to satiety by increasing the bulk of the food without increasing the total calorie intake.
- Prevent diverticulosis and reduce the risk of colonic cancer.
- Prevent increase in plasma cholesterol concentration by preventing absorption of cholesterol.
- Slow down gastric emptying.
- Flatten the glucose tolerance curve by preventing the intake of more calorie-rich foods. When food is taken without fibres, more glucose is absorbed which may raise the blood glucose levels. This results in abrupt rise of blood glucose levels in the blood. Thereby a steep rise of curve in the glucose tolerance test is seen.
- Glucose levels are lowered in diabetic patients.
- Increase the water holding capacity of the colonic contents by swelling and holding water.
- Bind bile salts.

Natural sources of fibre include vegetables, fruits and bran of cereal grains. Food like legumes, green leafy vegetables, whole fruits, unrefined foods like bran and sprouted seeds have a high content of fibres. Indian diet contains about 40 g of dietary fibres. Fibre content of some common food items is as follows:

- 1%–3%—whole wheat, coriander, carrot, brinjal, cauliflower, ladies finger, mango
- 3%–5%—ragi, pulses, groundnut, guava

An average daily intake of 200–300 mg/kg/day of dietary fibres is recommended in children. In adolescents and adults, 20–40 g/day is recommended.

PROTEINS

Proteins contribute to the structural component of all the body cells and the other biologically important

nitrogenous compounds in the body. Lack of proteins can hamper cellular growth and repair.

Proteins also contribute to the energy requirements of the body. When there is lack of dietary carbohydrates and fats, dietary proteins are used for energy production. If that is not enough, body proteins may be broken down to release energy. So, adequate amount of carbohydrates and fats in the diet is essential for the *protein-sparing effect* on dietary and body proteins.

Proteins are made up of 20 amino acids. Twelve of these amino acids are synthesised in the body. These are called non-essential amino acids. The remaining eight amino acids have to be obtained from dietary sources and are hence called essential amino acids (Box 5.10). Histidine is an essential amino acid for children. Arginine, cysteine and taurine are essential for low-birth-weight babies.

Quality of Proteins

The amount of essential amino acids in a protein determines its quality. Animal proteins are of higher quality as they contain most of the essential amino acids in right proportions (Table 5.23). Although proteins of plant origin are of lower quality, this can be overcome by pairing of plant proteins to balance the deficient amino acids. For example, wheat (cereals) is deficient in lysine and threonine and legumes (pulses) are deficient in methionine. When cereals and pulses are taken together, they complement each other and the deficiency is overcome. Egg contains all the essential amino acids, hence it is known as reference protein. It is also a complete protein. *Complete protein* is a protein that contains all essential amino acids in the same proportion as required by the human body. Other determinants of protein quality are discussed next.

BOX 5.10 Essential amino acids

Tryptophan
Methionine
Threonine
Isoleucine
Valine
Phenylalanine
Lysine
Leucine
Histidine (in children)

TABLE 5.23 Difference between Animal and Plant Proteins

Features	Animal Proteins	Plant Proteins
Quality	High	Poor
Digestibility	Good	Lower
Essential amino acids	Present	Deficient in one or other like lysine, methionine
Biological value (BV)	Biological value of an egg is 100	Cereals and pulses consumed together will have a BV of 65

Biological Value

Another measure of the quality of a protein is its *biological value (BV)*. The BV of a protein is the fraction of the retained nitrogen compared to the absorbed nitrogen. BV is calculated by the following formula:

$$BV = \frac{\text{Retained nitrogen}}{\text{Absorbed nitrogen}} \times 100$$

Table 5.24 gives the BV of some sources of protein. Egg protein has the highest BV.

Protein Efficiency Ratio

Protein efficiency ratio (PER) is defined as the gain in weight per unit weight of protein consumed over a period of time.

$$PER = \frac{\text{Weight gain (grams)}}{\text{Weight of protein consumed (grams) over a period of time}}$$

TABLE 5.24 Biological Value of Various Proteins

Source of Protein	Biological Value
Egg protein	96–100
Cow's milk	90
Rice	77
Fish	75
Meat	74
Wheat	66
Bengal gram	74

TABLE 5.25 Protein Efficiency Ratio of Various Proteins

Source of Protein	Protein Efficiency Ratio
Egg	3.8
Fish	3.5
Meat	3.2
Cow's milk	2.8
Rice	1.7
Wheat	1.3
Bengal gram	1.1

PER of some common food items is given in Table 5.25.

Digestibility Coefficient

Digestibility coefficient (DC) is the amount of absorbed nitrogen compared to the nitrogen present in the food.

$$DC = \frac{\text{Absorbed nitrogen}}{\text{Food nitrogen}} \times 100$$

Net Protein Utilisation

Net protein utilisation (NPU) is the amount of retained nitrogen to the nitrogen present in the food item. It is the product value of BV and DC.

$$NPU = BV \times DC$$

NPU can be calculated from the following formula:

$$NPU = \frac{\text{Retained nitrogen}}{\text{Food nitrogen}} \times 100$$

Average-quality proteins have NPU of 65%. High-quality proteins have NPU of >65% (Table 5.26).

Nitrogen Balance

When proteins are ingested, nitrogen is utilised for the body growth. If the excreted nitrogen is less than the ingested nitrogen, as happens in a normally growing child, it is known as *positive nitrogen balance*. If the loss is more, it is known as *negative nitrogen balance* ingested. It is important to maintain a positive nitrogen balance for normal growth. Nitrogen balance is determined by the following formula:

$$\text{Nitrogen balance} = \text{Ingested nitrogen} - (\text{urinary nitrogen} + \text{faecal nitrogen})$$

TABLE 5.26 Net Protein Utilisation of Various Proteins

Source of Protein	Net Protein Utilisation
Egg	96
Cow's milk	85
Rice	77
Meat	76
Fish	74
Bengal gram	61
Wheat	61

Functions of Proteins

- Tissue synthesis, maintenance and growth
- Regulation of body processes
- Source of energy—1 g will provide 4 kcal

FATS/LIPIDS

Fats are concentrates of energy composed of fatty acids. One gram fat provides 9 kcal of energy. Neutral fats are triglycerides with three fatty acids and one glycerol.

Fatty Acids

There are three types of fatty acids, depending on the saturation:

1. Saturated—the combining power of carbon atom is satisfied. Examples include palmitic and stearic acids
2. Monounsaturated—have only one point of unsaturation (e.g., oleic acid)
3. Polyunsaturated—have two or more points of unsaturation

On the basis of total number of carbon atoms present in the fatty acid, these are classified as follows:

1. Short-chain—contain 2–6 carbon atoms
2. Medium-chain—contain 8–14 carbon atoms
3. Long-chain—contain 16 carbon atoms and above up to 24 carbon atoms

Sources

1. Animal sources
   - Ghee

- Butter
- Margarine
- Egg yolk
- Cheese
- Cream whole milk

2. Plant sources
   - Mustard oil
   - Sesame oil
   - Nuts
   - Vegetable oils

The fat content of the food may be visible or invisible. Visible fat is present in the food items that are purchased as fats. It can be seen by naked eyes. Examples include oil, ghee, butter and margarine. Invisible fat or hidden fats cannot be seen by naked eyes and is present in nuts, vegetable oils, egg yolk, cheese, cream whole milk, etc. Amount of invisible fat present in some common food items is given in Table 5.27. The invisible fat content is roughly about 10%–15% of the total calorie intake. Hence, the visible fat intake in a healthy diet should constitute at least 20% of the total calories.

Absorption of Fats

The fat consumed is hydrolysed by salivary lipase and pancreatic lipase into fatty acids and monoglycerides.

Long-chain fatty acids and monoglycerides are absorbed in the intestinal mucosal cells by diffusion. There will be re-esterification of these fatty acids and monoglycerides into triglycerides. Triglycerides or neutral fats contain three fatty acids with one glycerol.

Short- and medium-chain fatty acids are hydrolysed by pancreatic enzymes to free fatty acids. In the absence of pancreatic lipase, these fatty acids are hydrolysed by mucosal lipase. There is no re-esterification or chylomicron formation. Rather they enter the blood directly through the intestinal veins.

Fats should contribute about 30%–40% of the energy in a healthy balanced diet.

TABLE 5.27 Fat Content in Common Food Items

Food Item	Amount of Invisible Fat (%)
Red gram	58
Bengal gram	65
Wheat	55
Rice	50

Functions of Fats

- Insulation—provides warmth
- Absorption of fat-soluble vitamins
- Act as a vehicle for absorption for vitamins A, D, E and K
- Source of essential fatty acids
- Protein sparing effect—when fats and proteins are taken in adequate quantities, the amount of proteins utilised for calorie production is reduced
- Condensed form of energy—1 g will provide 9 kcal

Essential Fatty Acids

Essential fatty acids (EFAs) are functional components of membrane lipids. EFAs are polyunsaturated fatty acids which are needed in the diet as the synthesis is not enough to meet the body needs. Polyunsaturated fatty acids include omega-6 fatty acids (e.g. linoleic acid) and omega-3 fatty acids (e.g. linolenic acid). The ratio of omega-6 fatty acids and omega-3 fatty acids should be 5:1 to 10:1. Food items like groundnut, safflower oils contain high omega-6 and low omega-3 fatty acids.

EFA requirement is 3% of total energy requirement of the child. Vegetable oils are rich in EFAs. The EFA content of some commonly used food products is depicted in Table 5.28. Poor sources of EFAs include saturated fats like ghee, hydrogenated fats and coconut oil. Coconut oil contains less of EFAs but it is rich in medium-chain triglycerides. Essential fatty acids are converted into long-chain fatty acids (Table 5.29). Deficiency of long-chain fatty acids results in dyslexia, dyspraxia and hyperactivity.

VITAMINS

Vitamins are organic nutrients that are required for a variety of biochemical functions. These nutrients,

TABLE 5.28 EFAs in Various Edible Oils (g/100 g)

Oil	Total EFA	Linoleic	Linolenic
Safflower	74.5	74	0.5
Soya bean	57	52	5
Sunflower	52	52	Traces
Corn oil	52	50	2
Cotton seed	50.7	50.3	0.4
Rice bran	34.6	33	1.6
Groundnut	28.3	28	0.3
Coconut	2.2	2.2	Nil
Palmolein	12.3	12	0.3
Ghee	2.1	1.6	0.5

generally, cannot be synthesised by the body and must therefore be supplied in the diet. Vitamins are classified into two groups:

1. Fat-soluble—vitamins A, D, E and K
2. Water-soluble—vitamins B and C

The daily requirements of vitamins in children of various age groups and the sources for obtaining them are given in Table 5.30.

Vitamin A

Vitamin A or retinol is obtained from the diet as

- carotene from plant sources and
- retinal from animal sources.

Out of the many different carotene pigments, the β-carotene yields the highest amount of retinol. Beta-carotene is also known as pro-vitamin A and gets converted into retinol in the intestinal wall. Both retinol and carotenes are fat-soluble. Cooking or frying in oil improves the absorption of carotenes.

Absorbed vitamin A is stored in the Ito cells of the liver as retinyl palmitate. These stores last for 6 months. Retinol is transported in the blood, bound to retinol binding protein (RBP).

Functions

- Maintenance and normal functioning of body tissues
- Maintains cellular integrity
- Enhances the immune competence and thus prevents infections

Vision. Rhodopsin or visual purple is a conjugated chromoprotein. It is composed of a protein scotopsin and a pigment, 11-cis retinene, which is present in the rod cells of retina. Rhodopsin is light sensitive and when light falls on the eye, it gets decomposed. 11-cis retinene is converted to 11-trans retinene and is split off from the scotopsin.

The enzyme retinene isomerase brings about the reverse reaction in darkness. Here 11-trans retinene is converted to 11-cis retinene which recombines with scotopsin to regenerate rhodopsin. Regeneration of rhodopsin is vitamin A dependent. Hence, patient with vitamin A deficiency has a defective dark adaptation.

Antioxidant Activity. Beta-carotene has antioxidant properties. This reduces the incidence of lung, breast, oral, oesophageal and bladder cancers.

Deficiency

Predisposing Conditions

- Celiac disease
- Tropical sprue
- Hepatic disorders
- Excess use of liquid paraffin

TABLE 5.29 EFAs as Precursors of Long-Chain Fatty Acids and the Sources

EFAs	Long-Chain Fatty Acids	Sources	
		Plants	Animals
Linoleic acid (an unsaturated omega-6 fatty acid)	Arachidonic acid Docosatetraenoic acid (adrenic acid)	Vegetable oils of safflower, poppy seed, corn oils	Breast milk
Linolenic acid	α-Linolenic acid, Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)	α-Linolenic acid and omega-3 fatty acid in flaxseed oil, canola, perilla, walnut oils	Omega-3 fatty acids in fish oil (EPA and DHA)

TABLE 5.30 Sources and Daily Requirement of Vitamins

Vitamins	Daily Requirements of Vitamins	Sources of Vitamins	
		Plant Sources	Animal Sources
Vitamin A	Under 1 year—1000–1500 IU 1–3 years—2000 IU 4–6 years—2500 IU 7–9 years—3500 IU 10–12 years—4500 IU	Dark green leafy vegetables, carrots, yellow fruits	Liver, meat, milk products, fish liver oil, cod liver oil, butter, egg yolk, whole milk
Vitamin C (ascorbic acid)	Infants—35 mg Preterm—50 mg Children—40–45 mg	Citrus fruits, drumstick leaves, tomatoes, cabbages, potatoes, green leafy vegetables, berries, germinating pulses	Liver, kidneys Negligible amount in adrenals
Vitamin D	Preschool—400 IU (10 µg) Older children—200 IU (5 µg)	Cereals	Milk, butter, egg yolk, fish liver oil (cod and halibut varieties)
Vitamin E	Infants—3–4 mg Children—6–7 mg Adolescents—5–15 mg	Cereals (whole meal), legumes, vegetable oils are the richest sources of vitamin E. Vegetable seed oil, germ oils of various seeds (rape seeds, corn, soya bean, wheat) palm, peanuts, nuts, cotton seed, sunflower, safflower, groundnuts Green leafy vegetables	Dairy products—milk, milk fat, egg, fish, meat, meat products, butter
Vitamin K	Infants • 0–6 months—15 µg/kg • 7–12 months—15–25 µg/kg Children • 1–3 years—30 µg/kg • 4–8 years—55 µg/kg • 9–13 years—60 µg/kg Adolescents • 14–18 years—75 µg/kg • >19 years—90 µg/kg	Green leafy vegetables, cabbages, spinach, alfalfa, tomatoes, soya beans	Pork liver is a good source; it is also synthesised in the colon
Vitamin B_1 (thiamine)	Infants—0.2–0.4 mg/day • 0–6 months—0.2 mg/day • 7–12 months—0.3 mg/day Children—0.5–1 mg • 1–3 years—0.5 mg • 4–8 years—0.6 mg • 9–13 years—0.9 mg Adolescents • >14 years—1–1.2 mg	Whole grain cereals, legumes, white bread, nuts, groundnut, oil seeds, dried yeast	Meat, milk, liver, pork
Vitamin B_6 (pyridoxine)	Infants—0.2–0.5 mg Children—0.5–1.5 mg Adolescents—1.5–2 mg	Whole grains, corn, soya beans, nuts, green vegetables, yeast, cereals, legumes	Liver, meat, kidney, fish
Vitamin B_{12} (cyanocobalamin)	Infants—0.3–0.5 µg Children—1–2 µg	Yeast extract	Milk, meat, egg, liver, kidney, cheese
Folic acid	Infants—25–35 µg Children—50–150 µg Adolescents—100–200 µg	Green leafy vegetables, legumes, peas, beans, nuts	Liver, meat, egg, kidney, cheese

(Table continued)

TABLE 5.30 *(Continued)*

Vitamins	Daily Requirements of Vitamins	Sources of Vitamins	
		Plant Sources	Animal Sources
Vitamin B_3 (niacin)	Infants—5–6 mg • 0–6 months—2 mg • 7–12 months—4 mg Children—6–12 mg • 1–3 years—6 mg • 4–8 years—8 mg • 9–13 years—12 mg Adolescents • >14 years—14–16 mg	Whole grains, green leafy vegetables, dried legumes, beans	Meat, fish, liver, eggs, yeast, kidney, heart
Vitamin B_5 (pantothenic acid)	Infants • 0–6 months—1.7 mg • 7–12 months—1.8 mg Children • 1–3 years—2 mg • 4–8 years—3 mg • 9–12 years—4 mg Adolescents • >13 years—5 mg	Most foods—cereals, legumes, molasses, wheat bran, peas, sweet potatoes, whole rye flour, mushroom, nuts	Meat, liver, kidney, egg, beef, yeast, saltwater fish, royal jelly
Vitamin B_2 (riboflavin)	Infants—0.5 mg/1000 kcal Children—0.6–1.2 mg/1000 kcal (0.025 mg/1 g protein intake)	Green leafy vegetables, whole grains, enriched grains	Meat, milk, egg, cheese, fish
Vitamin H (biotin)	Infants—20 µg Children—20–100 µg Adolescents—150–200 µg	Peanuts, yeast, cereals, legumes	Liver, egg yolk

Clinical Features

1. *Ocular Manifestations:* These include defective dark adaptation, night blindness, xerophthalmia (dry eyes), Bitot's spots, corneal xerosis, corneal ulceration and keratomalacia. Defective dark adaptation can be detected by dark adaptometry or electroretinography in the early stages before night blindness appears. WHO classification of signs of vitamin A deficiency is given in Box 5.11.

   (a) Conjunctival findings—the lesions occur characteristically in the bulbar conjunctiva.

   - Conjunctival xerosis—seen at the bulbar conjunctiva, lateral to limbus. The conjunctiva is dry and lacks normal lustre. The affected area becomes unwettable by tears. These are due to disruption of the continuity of the conjunctival epithelium.
   - Hazy conjunctiva—the conjunctiva appears hazy and leads to loss of transparency.
   - Thickening of conjunctiva—the affected area becomes thickened and rough. Wrinkling of the bulbar conjunctiva is seen in the lateral half of the eyes.
   - Pigmentation—guttural pigmentation is one of the early signs of vitamin A deficiency. This is seen in the lateral half of the bulbar conjunctiva.
   - Bitot's spots—is a small plaque of silver grey colour with a foamy surface. It is seen in the lateral half of the bulbar conjunctiva just close to the limbus. The shape is triangular, usually. The spots vary in size from 2 to 10 mm. These are usually seen bilaterally.

   (b) Corneal findings

   - Corneal xerosis—this occurs in later stages after the appearance of the conjunctival

BOX 5.11 WHO classification of vitamin A deficiency

Primary signs
- X1A—conjunctival xerosis
- X1B—Bitot's spots
- X2—corneal xerosis
- X3A—corneal ulceration/keratomalacia (less than one-third of cornea involved)
- X3B—corneal ulceration/keratomalacia (more than one-third of cornea involved)

Secondary signs
- XN—night blindness
- XF—fundal changes: xerophthalmic fundus
- XS—corneal scars

xerosis and Bitot's spots. The corneas of both eyes appear hazy. In most advanced cases, the cornea appears milky. This is due to cellular infiltration of the cornea. The changes can be reversed if the treatment is started at this stage.
- Corneal ulceration occurs if the child is not treated.
- Perforation of the eye with iris prolapse. This usually occurs in the lower and central part of the cornea.
- Keratomalacia—softening of the cornea involving a part or whole of the cornea. Later the lens may be extruded and loss of vitreous can happen. Secondary infections are common.

(c) Fundal changes (xerophthalmia fundus)—small white spots are seen on the retina. These do not interfere with vision.

2. *Skin changes:* The skin changes are due to fatty acid deficiency. The advanced eye changes may be present in the absence of skin changes. Also, the skin changes may be present without eye changes. Hence, it is suspected that factors apart from vitamin A are also responsible for skin changes.
   (a) The skin becomes dry due to the involvement of the glands in the skin.
   (b) Phrynoderma is a skin disorder which results in follicular keratosis. It occurs due to plugging of hair follicles by keratotic plugs which consist of keratinised epithelium projecting outwards from the follicles. The skin becomes scaly and toad like. This is usually seen on the outer side of the legs, buttocks, elbow and back of the forearm (Fig. 5.3).



FIGURE 5.3 Phrynoderma on elbow due to the deficiency of vitamin A.

3. *Respiratory tract:* Squamous metaplasia of the respiratory mucosa and ciliary damage occurs. The children are prone to respiratory infections.
4. *Gastrointestinal system:* Changes in the intestinal mucosa lead to recurrent diarrhoea.
5. *Reproductive system*: Atrophy of germinal epithelium.
6. *Growth:* The skeletal involvement may result in growth retardation.
7. *Immunological system:* Decreased immune response.

Treatment

Vitamin A deficiency is treated by administration of vitamin A.

- < 6 months—50,000 IU
- 6–12 months—1,00,000 IU
- >1 year—2,00,000 IU

The above mentioned doses are given orally on day

1 and day 2. The same dose is repeated again after 2–4 weeks.

National Vitamin A Prophylaxis Programme

Vitamin A supplementation programme has been in operation in India since 1970. This programme is sponsored by the Ministry of Health and Family Welfare (Government of India). Under this programme, children between 9 months and 3 years are given 6 monthly doses of vitamin A. The administration of the first two doses is linked with routine immunisation. At 9 months, 1,00,000 IU dose of vitamin A is given orally along with measles vaccination. Subsequently, 2,00,000 IU dose is given orally every 6 monthly till the age of 3 years. Vitamin A deficiency is rare after 3 years of age so this prophylaxis is not continued after 3 years.

Vitamin A Supplementation for Sick Children.

All children suffering from measles are given one dose of vitamin A if they have not received it in the previous 1 month. All cases of severe malnutrition are given one additional dose of vitamin A.

Hypervitaminosis A

This is due to excessive intake of vitamin A containing solutions or therapeutic overdose. Excess intake of carotenoids does not result in toxicity.

1. Acute toxicity (acute hypervitaminosis A)
   - Headache and dizziness
   - Nausea
   - Vomiting
   - Abdominal pain
   - Pseudotumour cerebri (bulging anterior fontanel)
2. Chronic toxicity (chronic hypervitaminosis A)
   - Anorexia
   - Dry skin
   - Pruritus
   - Sparse hair
   - Bone pains
   - Benign intracranial hypertension
   - Weight loss
   - Hepatosplenomegaly
   - Hypoplastic anaemia
   - Desquamation of skin

Vitamin D

Vitamin D Deficiency

Vitamin D deficiency can lead to rickets (refer Chapter 9). Causes for deficiency are

- decreased exposure to sunlight and
- inadequate intake of vitamin D.

Hypervitaminosis D

It is due to excess intake of vitamin D. Its clinical features are as follows:

- Anorexia, nausea and vomiting
- Constipation
- Hypertension
- Clouding of cornea
- Drowsiness, irritability and hypotonia
- Polyuria (increased urination) and polydipsia (increased thirst)
- Renal damage
- Hyperkalaemia
- Metastatic calcification in kidneys, lungs, arteries and soft tissues

Investigations

- Serum calcium—hypercalcaemia (15–20 mg/dL); may rise up to 30 mg/dL
- Urine for calcium—hypercalciuria
- Urine for proteins—proteinuria

Treatment

- Decrease the intake of vitamin D
- Oral aluminium hydroxide
- Cortisone
- Sodium versenate

Vitamin E

Vitamin E is an antioxidant which prevents free oxygen radicals-induced peroxidase damage to the cells.

Daily Requirement

The daily intake should be 3–10 mg of α-tocopherol. Intake of 1 mg of α-tocopherol provides 1.5 IU activity of vitamin E. Recommended daily intake is 4 IU for infants and 15 IU for adolescents. The requirement is related to polyunsaturated fat intake.

Vitamin E Deficiency

The body cells are prone to be damaged. The following features are seen:

- Haemolytic anaemia
- Muscle weakness and myopathy
- Neuropathy, ataxia due to posterior column degeneration, diminished or absent deep tendon reflexes
- Dysarthria
- Ptosis, ophthalmoplegia and pigmented retinopathy may occur
- Hyperbilirubinaemia and intraventricular haemorrhage are seen in preterm infants with vitamin E deficiency

Treatment

- 100 mg of vitamin E IM for several days.

Vitamin K

Coagulation factors II, VII, IX and X are vitamin K-dependent.

Sources

- Plant sources—green leafy vegetables, cabbages, spinach, tomato, soya beans
- Animal sources—liver

Vitamin K is synthesised in the gut by the microorganisms in the gut. It is a fat-soluble vitamin and bile is required for absorption in the gut. Breast milk is a poor source of vitamin K.

Deficiency

Predisposing Factors

A	Antibiotics used for prolonged periods decrease the intestinal flora and thereby synthesis of vitamin K
B	Biliary obstruction
C	Cirrhosis and cystic fibrosis
D	Drugs—salicylates and sulphonamides
E	Exclusive breastfeeding
F	Fat malabsorption
G	Gastroenteritis

Clinical Features

- Haemorrhage
- Haemorrhagic disease of newborn

Treatment

For haemorrhagic disease of newborn, vitamin K is given as

- 1–2 mg orally daily for infants,
- 5 mg IM for bleeding until bleeding is controlled.

For prophylaxis in a newborn, 0.5–1 mg vitamin K is given IM at birth.

- 1 mg for babies weighing >2 kg
- 0.5 mg for babies weighing <2 kg

Vitamin K Excess

This usually occurs in newborn babies. Effects are as follows:

- Haemolytic anaemia
- Hyperbilirubinaemia and kernicterus
- Hepatomegaly

Vitamin B_1 (Thiamine)

Functions

Thiamine pyrophosphate (TPP) is the active form of vitamin B_1. It is required as a cofactor for several important enzymes required during carbohydrate metabolism—pyruvate dehydrogenase and α-ketoglutarate dehydrogenase. These two enzymes catalyse oxidative decarboxylation.

Transketolase is also dependent on TPP. It is an enzyme of the pentose pathway.

Deficiency

Consumption of diet mainly consisting of polished rice results in thiamine deficiency. It is also common in children with malnutrition, persistent vomiting and adults with alcohol abuse. This results in beriberi.

Wet beriberi is associated with cardiovascular system involvement. Signs of congestive cardiac failure such as palpitations, tachycardia, dyspnoea and oedema are present.

Dry beriberi is associated with nervous system involvement and Wernicke's encephalopathy. Its clinical features include the following:

- Apathy, confusion, depression and drowsiness
- Anorexia
- Ataxia
- Altered behaviour and emotional disturbances
- Constipation
- Wernicke's encephalopathy
- Korsakoff's psychosis
- Fatigue
- Growth failure
- Getting up from sitting position difficult due to calf muscle tenderness
- Headache, irritability and insomnia
- Diminished or lost tendon reflexes
- Muscle atrophy and weakness
- Numbness/tingling sensations of the legs
- Ophthalmoplegia
- Polyneuritis and peripheral neuropathy (ascending, symmetrical)

Infantile beriberi is seen in infants of mothers with thiamine deficiency and it is of three types—cardiovascular, aphonic and neurologic. Age of onset is 2–3 months. They may present with features of both wet and dry beriberi.

Wernicke–Korsakoff syndrome is seen in thiamine deficiency and is a combination of Wernicke's encephalopathy and Korsakoff's psychosis.

1. Wernicke's encephalopathy (due to acute severe deficiency of thiamine)
   - Irritability
   - Somnolence
   - Mental confusion
   - Progressive mental deterioration
   - Ataxia
   - Permanent memory defect
   - Ocular signs—bilateral symmetrical ophthalmoplegia (weakness or paralysis of eye movements), abnormal pupillary reflexes, nystagmus
   - Coma
2. Korsakoff's psychosis (due to chronic deficiency of thiamine)
   - Amnesia
   - Confabulation
   - Disorientation
   - Defects in memorising, especially new information
   - Learning difficulties

Investigations

- Red blood cell transketolase activity—decreased
- 24-hour urinary thiamine excretion

Treatment

- Dry beriberi is treated with thiamine hydrochloride 100 mg IM single dose or 25 mg IM for 3 days. This is followed by 10 mg, orally twice daily for next 5 days and then 10 mg/day orally for next 6 weeks.
- Wet beriberi is treated with oral or parenteral thiamine. Thiamine 10–30 mg is given intravenously followed by 10 mg, orally twice daily for next 5 days. This is followed by 5–10 mg/day orally for 6 weeks. Within few hours of thiamine administration, there is diuresis resulting in resolution of oedema.
- Infantile beriberi—mother should be treated with 50 mg orally daily if she is breastfeeding and the baby is suffering from beriberi.
- Wernicke's encephalopathy should be treated immediately with intravenous thiamine hydrochloride in a dose of 50 mg. This should be followed by 50 mg IM twice a day for 1 week.

Prevention

Eating of parboiled rice should be encouraged. Milled rice lacks thiamine and should be avoided.

Adverse Effects

Large doses of thiamine given parenterally can result in anaphylactic shock.

Vitamin B_2 (Riboflavin)

It plays a vital role in cellular oxidation. The active form of riboflavin plays an important role in oxidation of carbohydrates and amino acids.

Deficiency (Ariboflavinosis)

Clinical Features

The deficiency symptoms are seen mainly in skin and mucosae.

1. Angular stomatitis or cheilosis—fissuring and ulcerations at the angle of mouth
2. Glossitis—sore, red, glazed and smooth tongue (magenta tongue). There is atrophy of the lingual papillae

3. Dyssebacia—plugging of the sebaceous glands. The areas commonly affected are nasolabial folds, alae nasi, external ears, eyelids, scrotum in the male and labia majora in the females
4. Eyes
   - Vascularisation of cornea
   - Cataract
   - Keratitis
   - Watering of eyes with photophobia
5. Scrotal and vulval dermatitis—patchy redness is seen early and may progress to scaling and desquamation
6. Growth retardation
7. Non-specific features—anorexia and weight loss

Investigations

- 24-hour urinary excretion of vitamin.
- Activity of glutathione reductase in erythrocytes is a functional index of flavin coenzyme activity.

Treatment

Riboflavin 3–10 mg should be given daily in 2–3 divided doses for few days, until symptoms improve. If there is no improvement, 2 mg of riboflavin in saline can be infused three times a day. This should be followed by 10 mg orally for 3 weeks.

Vitamin B_3 (Niacin)

Nicotinic acid and nicotinamide are both referred to as niacin. Nicotinamide adenine dinucleotide and its phosphates (NAD and NADP) are essential as coenzymes in oxidation–reduction reactions. Niacin is needed for normal functioning of nervous system, skin and gastrointestinal system.

Sources

Common sources are liver, kidney, yeast, meat, whole milk, cereals, vegetables and pulses. In cereals, especially maize, the greater part of vitamin is bound and cannot be absorbed. It can be liberated from the bound form by treatment with alkali. The human body can synthesise this vitamin from tryptophan. On an average, 1 mg of nicotinic acid is synthesised from 60 mg of tryptophan.

Deficiency

Causes of deficiency are as follows:

- Decreased intake
- Tryptophan-deficient diet as in maize
- Hartnup disease (disorder of tryptophan metabolism due to defect in the transport of neutral amino acids by the intestinal mucosa and renal tubules)
- Increased catabolism of niacin as in carcinoid syndrome

Clinical Features

Deficiency of niacin results in pellagra (3 Ds—diarrhoea, dermatitis and dementia). It affects the following:

1. Gastrointestinal system—diarrhoea, nausea, excessive salivation and epigastric pain
2. Tongue—beefy-red in colour, swollen, painful and devoid of papillae (fiery-red tongue)
3. Neurological manifestations—muscle weakness, irritability, mental retardation, loss of memory, delirium or dementia. The spinal cord involvement leads to spastic paraplegia. Paraesthesia and peripheral neuropathy can occur
4. Skin—dermatitis on the parts of the body exposed to sunlight. Redness and thickening is followed by hyperkeratosis. There is desquamation, leaving hypopigmented patches. The lesions are hyperpigmented, symmetrical and affect both sides of the body. Depending upon the site of lesions, the lesions are:
   - Casal's necklace—around the neck
   - Pellagra glove—forearm and hand
   - Pellagra boot—legs are involved
5. Haematological manifestation—anaemia

Investigations

- Peripheral blood smear—macrocytic anaemia
- NAD, NADP and nicotinic acid levels in the blood—decreased.
- Excretion of metabolites of nicotinic acid and tryptophan in urine—decreased

Treatment. Nicotinamide is preferred over nicotinic acid for oral therapy. It is given in a dose of 100–150 mg/day orally in 3 divided doses.

Niacin is given intravenously in severe cases and in malabsorption.

As the skin lesions in niacin deficiency are aggravated by sunlight, it is important to prevent exposure to sun and apply cream over the exposed parts.

Niacin deficiency can be prevented by fortification of food items like bread with nicotinic acid.

Toxicity Due to Nicotinic Acid Excess

- Flushing
- Giddiness
- Intense burning sensation of skin
- Jaundice (cholestatic)

Vitamin B_6 (Pyridoxine)

There are three active forms:

- Pyridoxine
- Pyridoxal
- Pyridoxamine

Pyridoxal phosphate participates in reactions like transamination, decarboxylation, deamination, transsulfuration, condensation for protein and fat metabolism. It is destroyed by ultraviolet rays and heat.

Recommended Intake

- Infants—0.3 mg/day
- Adults—1–2 mg/day

Toxicity results in sensory neuropathy.

Deficiency

Dietary deficiency is rare. Metabolic disorders are common. The following drugs predispose to pyridoxine deficiency:

- INH given for tuberculosis depletes the tissues of pyridoxine by combining with pyridoxal or pyridoxal phosphate to form metabolically inactive hydrazone derivatives. These inhibit pyridoxal phosphate-dependent enzymes.
- Estrogens block the coenzyme in tryptophan metabolism.
- Penicillamine combines with pyridoxal phosphate to form a metabolically inactive product.
- Cycloserine is a pyridoxine antagonist.

Clinical Features

- Microcytic hypochromic anaemia refractory to iron therapy
- Hyperirritability
- Convulsions
- Peripheral neuropathy
- Growth retardation
- Cheilosis/angular stomatitis
- Glossitis
- Skin lesions—seborrhoeic dermatitis around eyes, nose and mouth

Investigations

- In a child who presents with convulsions due to pyridoxine deficiency, EEG shows myoclonus with hypsarrhythmic pattern. If seizures are controlled by pyridoxine 100 mg IM, its deficiency is suspected.
- Hypochromic, microcytic anaemia responding to pyridoxine. The child responds to the normal requirement dose.
- Tryptophan load test—urinary excretion of xanthurenic acid is increased after loading a pyridoxine-deficient child with 100 mg/kg of tryptophan. Xanthurenic acid becomes normal after administration of large doses of vitamin B6. In some normal children, xanthurenic acid may be found in urine. In cases with pyridoxine dependency, this test is normal.

Treatment

Deficiency is corrected by administration of pyridoxine 5 mg IM followed by 0.5 mg orally for 2 weeks. It is given in the following oral doses to prevent deficiency.

- Infants—0.3–0.5 mg
- Children—0.5–1.5 mg
- Adolescents—1.5–2 mg

Vitamin B_6-Dependent Conditions

Dependency is a condition where the child requires large quantities of vitamin. The symptoms do not improve with usual dose of vitamins. This may be due to abnormal pathways of B_6 or tryptophan metabolism. The vitamin B_6-dependent conditions are as follows:

- B_6-dependent convulsions
- B_6-dependent anaemia

Dose in pyridoxine-dependent cases—2–10 mg IM or 10–100 mg orally daily.

Vitamin B_{12} (Cyanocobalamin)

Its functions are as follows:

- It helps in synthesis of nucleic acid along with folic acid.
- It is essential for formation and maturation of red blood cells.
- It maintains normal activity of nervous system.

Vitamin B_{12} is absorbed in the lower part of the ileum.

Sources

It is a vitamin that is synthesised by microorganisms and is not found in plants. The children are dependent on the animal sources (liver, kidneys and meat). Strict vegans who do not consume milk or milk products are prone to develop its deficiency.

Deficiency

Deficiency of this vitamin can be primary or secondary.

1. Primary deficiency—decreased intake
2. Secondary deficiency
   - Inadequate absorption (Addisonian pernicious anaemia due to failure of secretion of intrinsic factor in the stomach, after resection of stomach results in intrinsic factor deficiency, diseases of terminal ileum, bacterial colonisation of small intestine)
   - Inadequate utilisation of the vitamin B_{12}
   - Increased requirement of this vitamin
   - Increased excretion—due to inadequate binding of this vitamin in the serum. This occurs in liver and kidney diseases

Clinical Features

- CNS—irritability, convulsions, retrobulbar neuropathy, subacute combined degeneration due to involvement of the posterior column, mental retardation
- Haematological system—megaloblastic anaemia, pernicious anaemia (due to defect in absorption of vitamin B_{12}, small bowel diseases, drugs such as para-aminosalicylate sodium [PAS] and neomycin)
- Skin—hyperpigmentation of the knuckles and nail beds
- Bald tongue

Investigations

Schilling Test. Fasting child is given 1 µg of radiolabelled vitamin B_{12} orally in 20–50 mL of water. Along with this 1000 µg of flushing dose of unlabelled B_{12} is given parenterally. This large dose flushes out the radioactive vitamin B_{12} from the body. Urine is collected for 24 hours. Normal excretion is about 0.3 µg (30% of the given dose) of radiolabelled vitamin B_{12}. This test is used to differentiate between the dietary deficiency and intrinsic factor deficiency, when excretion is abnormal and can be corrected by oral intrinsic factor.

Modified Schilling Test. The radioactive vitamin B_{12} is given along with 30 mg of intrinsic factor. In intrinsic factor deficiency, the test becomes normal. If the pathology is in the ileum (intestinal malabsorption), the excretion is abnormal and cannot be corrected by oral intrinsic factor.

Treatment

A total of 100 µg of cyanocobalamin or hydroxycobalamin is given three times a week till the haemoglobin is normal. Following this the child is given 100 µg IM weekly and then monthly.

When associated with neurological complications, the dose can be increased to 500 µg. A reticulocyte peak occurs within a week after the treatment is started.

Folic Acid

Folic acid occurs naturally as folates, which are reduced with increased temperature and storage and cooking. Its functions are as follows:

- Synthesis of purines and pyrimidines for nucleic acid synthesis along with vitamin B_{12}.
- Breakdown of histidine.
- Interconversion of amino acids such as serine and glycine.
- Prevention of preterm delivery, placental abruptions and infarctions. It also causes increase in birth weight.

- Protection against development of atherosclerosis and vascular diseases due to homocysteine lowering effect.

Sources

- Vegetable sources—green leafy vegetables (spinach, broccoli), legumes, cereals peas, beans, nuts, yeast, fruits
- Animal sources—liver, meat, egg, kidney, cheese

Deficiency

Causes of folic acid deficiency are as follows:

- Dietary deficiency
- Malabsorption due to disease of proximal small bowel where it is mainly absorbed
- Folic acid antagonists such as anticonvulsants, INH and nitrofurantoin
- Infestation with fish tapeworm
- Increased demand in conditions with increased cell proliferation such as haemolytic anaemia and pregnancy

Clinical Features

- Anorexia
- Weakness
- Anaemia
- Diarrhoea
- Ulcers
- Glossitis (painful tongue)
- Impaired immunity
- Thrombosis (due to increased homocysteine levels)
- Folic acid deficiency in pregnant mothers predisposes to neural tube defects (spinal dysraphism, meningomyelocele) in the babies

Investigations

- Megaloblastic anaemia
- Serum and red blood cell folate levels are low. This reflects in blood by 3 months. Hence in acute cases, the level may be normal
- Urinary formiminoglutamic acid (FIGLU) excretion test—an increased excretion of the urinary FIGLU following histidine loading

Treatment

- Folic acid 0.5–1.0 mg/day for 3–4 weeks is given orally or parenterally.
- Response is seen as increased reticulocyte count initially followed by increase in haemoglobin.
- Intake of folate results in rapid utilisation of vitamin B_{12}. Hence, it should not be given alone in any condition associated with vitamin B_{12} deficiency.

Prevention

Supplementation of folate to pregnant women in a dose of 0.4 mg/day. This should be started before pregnancy and should be continued for 3 months after the delivery of the child.

Vitamin H (Biotin)

Biotin acts as a coenzyme for carboxylases which are necessary for urea formation, biosynthesis of pyrimidines and fatty acids.

Sources

- Peanuts, yeast, cereals, legumes
- Liver, egg yolk
- Synthesised in the intestines by microorganisms. This may be affected by administration of sulpha drugs

Deficiency

Predisposing Factors

- Biotin deficiency occurs in children who consume large amounts of raw egg white which is rich in avidin, a biotin-binding glycoprotein.
- Prolonged parenteral hyperalimentation—Biotin is produced by microorganisms in the gastrointestinal tract.

Clinical Features

M	Muscle pain
A	Anorexia
L	Lassitude
A	Anaemia (mild)
I	Increased cholesterol
SE	Seborrhoeic dermatitis Sensations like burning, pricking—paraesthesia

Treatment. 0.5–2 mg/day orally or parentally.

Vitamin B_5 (Pantothenic Acid)

Functions of pantothenic acid are exerted through coenzyme A.

1. It is essential for metabolism of fats, carbohydrates and proteins.
2. It is essential for biosynthesis of haemoglobin.
3. Protein-bound pantothenic acid is required for biosynthesis of fatty acids. It prevents premature greying of hair, wrinkling of skin and plays an important role in secretion of hormone cortisone.

Sources

- Plant sources—cereals, legumes, molasses, wheat bran, peas, sweet potatoes
- Animal sources—meat, liver, kidney, egg

Vitamin B_5 is lost by cooking

Daily Requirement

Not known but less than 5 mg is enough. Daily diet contains 10 mg/day which is sufficient. The recommendations are as follows:

1. Infants
   - 0–6 months—1.7 mg/day
   - 7–12 months—1.8 mg/day
2. Children
   - 1–3 years—2 mg/day
   - 4–8 years—3 mg/day
   - 9–12 years—4 mg/day
3. Adolescents—5 mg/day

Deficiency

Deficiency is extremely rare and occurs in cases with severe starvation. Deficiency usually occurs in association with other vitamin deficiencies.

Clinical Features

Deficiency can cause the following features:

A	Alopecia
B	Burning feet syndrome (Gopalan's feet)
C	Cornification of skin
D	Depigmentation of hair Degeneration of spinal cord and peripheral nerves
E	Emesis—vomiting and nausea Eyes—keratitis Excessive sleep
F	Fatigue
G	Gastrointestinal disturbances—nausea, abdominal cramps and flatulence Growth arrest
H	Headache Hypofunction of adrenal cortex (adrenal haemorrhage)
I	Irritability

Investigations

- Increased insulin sensitivity
- Low blood cholesterol
- Decreased serum potassium

Vitamin C (Ascorbic Acid)

The deficiency of vitamin C was first observed in travellers sailing in a ship where the facilities for intake of fresh fruits were not available. The condition improved with the intake of fresh lemons and oranges. Functions of vitamin C are as follows:

- Regulation of oxidation–reduction reactions
- Carbohydrate and tyrosine metabolism
- Collagen and bone formation
- Conversion of folic acid to folinic acid
- Through its reducing property, it helps in iron and haemoglobin metabolism
- Synthesis of bile acid from cholesterol
- Synthesis of corticosteroids
- Cellular respiration (electron transport chain)

Sources

- Fresh fruits, mainly citrus fruits, lemon, orange, drumstick leaves, tomatoes, cabbage, potatoes, green leafy vegetables, berries
- Negligible amount in adrenals

Recommended Intake

- Infants—35 mg/day
- Children—40–45 mg/day

Deficiency

Clinical Features. Deficiency of vitamin C can

lead to scurvy. Scurvy can be infantile or childhood. Functions of osteoblasts and odontoblasts are impaired. Carbohydrate metabolism is abnormal. The features of deficiency of vitamin C are as follows:

- Frog posture due to pseudoparalysis—pain in bones and joints/generalised tenderness
- Irritability
- Spongy swelling of oral mucosae
- Scorbutic rosary—beading of the costochondral junction is due to the separation of epiphysis. The junction is angulated due to posterior displacement of the sternum. This part is tender
- Haemorrhages (due to increased fragility of capillaries)—orbital and subdural haemorrhages, bleeding gums (seen during the eruption of teeth), petechiae, haematuria, melaena, bleeding from internal organs
- Enlarged and prominent hair follicles
- Brittle bones
- Skin—dermal eruptions, follicular keratosis
- Increased susceptibility to infections
- Poor wound healing

Investigations

1. Anaemia
2. Delayed blood clotting
3. Serum ascorbic acid level is less than 0.1 mg/100 mL. Normal level is >0.6 mg/dL
4. Vitamin C content of the WBC is a sensitive indicator for the total body levels. Normal level is 25–40 mg/100 mg. Vitamin C level in the buffy coat of centrifuged blood is less than 0.1 mg%
5. Vitamin C excretion test. Test dose of vitamin C is given parenterally. Its excretion is measured in the urine collected over 3–5 hours after the loading dose. In scurvy due to vitamin C deficiency, less than 80% of the loading dose is excreted
6. X-ray (Fig. 5.4)
   - Generalised osteoporosis
   - Epiphysis surrounded by rarefied body and thick cortex gives an appearance of signet ring
   - Ground glass appearance
   - Cortex is thin (pencil point thinness)
   - Subperiosteal haemorrhage
   - White line of Frankel—a zone of well-calcified cartilage in the provisional zone of calcification with adjacent area of rarefaction known as area of rarefaction
   - Corner sign—the zone of well-calcified cartilage projects beyond the limits of the shaft
   - Wimberger's line—increased zone of calcification around the epiphysis
   - Scurvy line
   - Fragmentation above the calcified cartilage

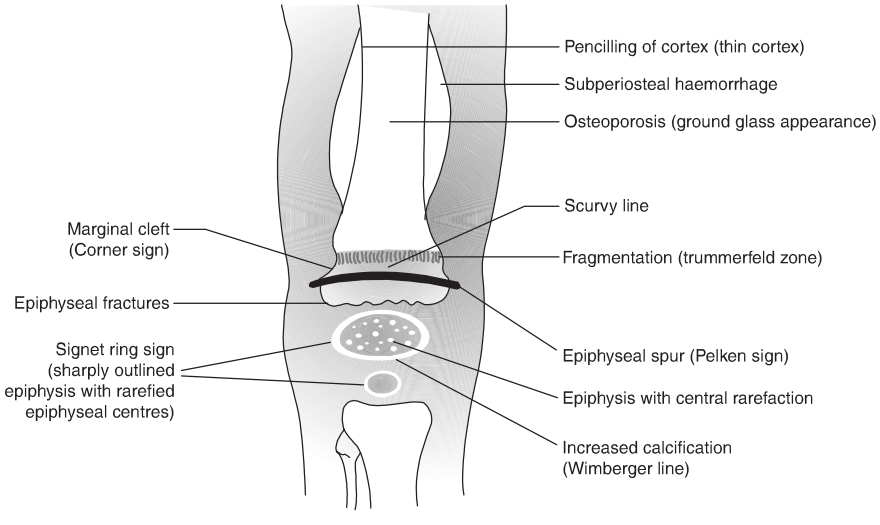


FIGURE 5.4 Radiological features in scurvy.

in the metaphysic—Trummerfeld zone
- Pelken's sign
- Epiphyseal fractures

Treatment
- 100–200 mg/day of ascorbic acid orally or parenterally for a week. Loading dose of 500–1000 mg/day orally may be needed for a week.

Prevention
- Intake of diet rich in vitamin C 50–75 mg/day.

MINERALS

Minerals are substances required in small quantities for the normal growth and functioning of the body. These are essential for a wide range of body functions such as regulation of enzyme metabolism, acid–base balance, nerve and muscle and skeletal integrity. For example, calcium and phosphorus are required for mineralisation of bones; magnesium is essential for various metabolic functions.

Minerals (macrominerals and trace elements)

Macrominerals	Trace elements
Required in relatively larger amounts	Required in small quantities
Calcium	Aluminium
Phosphorus	Arsenic
Magnesium	Chromium
Sodium	Cobalt
Potassium	Copper
Chloride	Fluoride
Sulphur	Iodine
	Iron
	Lead
	Manganese
	Molybdenum
	Mercury
	Nickel
	Selenium
	Silicon
	Vanadium
	Zinc

Sources, daily requirements and deficiency symptoms of some important minerals are given in Table 5.31. Excess intake of minerals may result in certain disorders in the body. These are given in Table 5.32.

Zinc

Zinc is a constituent of carbonic anhydrase and carboxypeptidase. Carbonic anhydrase is present in the red blood cells. It is essential for carbon dioxide exchange. Carboxypeptidase is present in the intestine. It is required for hydrolysis of proteins. Intake of whole grains decreases the absorption of zinc due to interference with phytates.

Deficiency

Clinical Features (see Fig. 5.5)

H	Hepatosplenomegaly Hyperkeratosis Hypermobility of joints due to defects in connective tissues and rib cartilage
A	Acrodermatitis enteropathica (alopecia, chronic diarrhoea, skin lesions) Anorexia Acral dermatitis
P	Pigmentation of skin (hyperpigmentation) Preterm delivery Pectus excavatum/carinatum
P	Poor wound healing Physical development delayed Puberty delayed in adolescents Poor appetite
I	Impaired taste Iron deficiency anaemia Immunity reduced (atrophy of thymus) Increased susceptibility to infections Intrauterine growth retardation, dwarfism
N	Neurological manifestations like depression, mental lethargy, behavioural changes Neural tube defects in the foetus (congenital defects related to nerve growth factor) Night blindness
E	Eczema Endocrine—hypogonadism (in chronic deficiency) Eye—cataract, myopia, retinal detachment, glaucoma, macular degeneration
S	Special senses—loss of taste and smell sensation Skin rough, striae
S	Short stature (in chronic deficiency) Sexual development delayed

TABLE 5.31 Minerals and Their Sources, Requirements and Deficiency Symptoms

Trace Elements	Deficiency Symptoms	Sources	Recommended Daily Intake
Iron	Anaemia (hypochromic and microcytic), growth failure	Jaggery, ragi, dates, green leafy vegetables, dates, amaranth, mint, whole grains, legumes, nuts, liver, meat, egg yolk	1–3 years—11–12 mg 4–6 years—18–19 mg 7–9 years—26 mg 10–12 years—34 mg
Calcium	Tetany	Milk, cheese, green leafy vegetables, ragi, oysters, egg	0–6 months—360 mg 6–12 months—540 mg 1–10 years—0.5–1 g >10 years—1.1–1.5 g
Phosphorus	Rickets	Milk, milk products, egg yolk, legumes, nuts, whole grains	Breastfed infants—25–30 mg/kg/day 0–6 months—540 mg 6–12 months—770 mg/day 1–10 years—880 mg/day >10 years—1200 mg/day
Zinc	Acrodermatitis enteropathica, dwarfism, hyperpigmentation, hypogonadism, poor wound healing, immunodeficiency	Grains, nuts, cheese, meat, oysters	5–15 mg/day 0–12 months—5 mg/day 1–10 years—10 mg/day >11 years—15 mg/day
Copper	Neutropenia, hypochromic refractory anaemia, osteoporosis, ataxia, hypopigmented hair	Liver, oysters, meat, fish, legumes, nuts, whole grains	0.05–0.1 mg/kg/day
Selenium	Keshan's disease (cardiomyopathy), decreased fertility	Vegetables, meat, garlic, grains	10–100 µg 0–12 months—10 µg 1–6 years—20 µg 7–10 years—30 µg
Iodine	Endemic cretinism, goitre	Seafoods, iodised salts	50–150 µg/day 0–6 months—40 µg 6–12 months—50 µg 1–3 years—70 µg 4–6 years—90 µg 7–10 years—120 µg
Chromium	Glycosuria, hyperglycaemia, encephalopathy, peripheral neuropathy	Yeast, liver, cereals, pulses, nuts, vegetables, fruits	2.5 µg/kg
Manganese	Increased bleeding and seizure disorders	Cereals, legumes, nuts, green leafy vegetables, whole grain	Normal diet contains 2 mg which is enough
Magnesium	Tetany (calcium-resistant), hyperexcitability, convulsions	Cereals, legumes, nuts, meat, milk	40–340 mg Infants—70–250 mg 1–4 years—200 mg 4–10 years—250 mg
Fluoride	Dental caries, osteoporosis	Water, sea foods, toothpaste	Water should contain 1–2 parts by million (100–200 µg/dL)
Sodium	Hypotension, muscle cramps	Table salt, milk, egg	2–3 mEq/kg
Potassium	Abdominal distension, ileus, flaccid paralysis	Fruits, vegetables, tender coconut, whole grains and cereals	2–3mEq/kg

TABLE 5.32 Effects of Mineral Excess

Minerals	Effects of Excess	Predisposing Factors
Fluoride	Fluorosis, mottling of teeth	Intake >4–8 mg/24 hours
Copper	Cirrhosis	Increased copper in the diet
Iron	Haemosiderosis, poisoning	Blood transfusion in haemolytic anaemia
Calcium	Heart block, renal stones	Parenteral calcium
Cobalt	Cardiomyopathy, goitre Cobalt polycythaemia due to stimulation of erythropoietin	Increased intake
Manganese	Encephalopathy, leg cramps, asthaenia	Chronic inhalation
Phosphorus	Tetany	Renal failure, excess intake of vitamin D
Potassium	Heart block, periodic paralysis	Intravenous infusion of potassium, cell injury, renal failure
Magnesium	Hyporeflexia, respiratory depression, drowsiness, coma	Renal failure In newborn when mother received intramuscular magnesium sulphate
Sodium	Oedema	Excess intake
Chromium	Dermatitis, renal failure	Excess intake



FIGURE 5.5 Acrodermatitis enteropathica due to zinc deficiency. The child presented with 2-year history of chronic diarrhoea.

Treatment

- 10 mg (2–6 months age) and 20 mg (>6 months age) of elemental zinc given for 14 days.

Iron

Iron is absorbed in ferrous form from the gut. It is transported in the blood as ferric form attached to transferrin. Monoamine oxidase is an iron-dependent enzyme which plays an important role in neurochemical reaction in the CNS.

Deficiency

It occurs due to either decreased intake or decreased absorption and increased loss.

Clinical features

- Hypochromic, microcytic anaemia
- Growth retardation (refer Chapter 13, section *Iron Deficiency Anaemia*, page 665)

Treatment

- 6 mg/kg in 2 divided doses for 3 months

Calcium

Calcium is present in the blood and bones. In the blood, the calcium is seen in both free ionised form and bound to serum protein. Normal calcium level in the blood is 9–11 mg/dL. About 6 mg/dL is bound to protein.

Functions

- Formation of bones
- Muscle contraction
- Transmission of nerve impulses
- Blood coagulation—essential for conversion of prothrombin to thrombin
- Integrity of intracellular cement substance

Hypocalcaemia

Predisposing Factors

- Acute pancreatitis
- Bowel disorders—chronic diarrhoea
- Chronic renal failure
- Decreased intake
- Excess cereal intake—phytic acid
- Fat malabsorption—steatorrhoea
- Glomerulonephritis—chronic
- Hypoparathyroidism
- Hypoproteinaemia
- Inadequate intake or absorption of calcium
- Birth asphyxia
- Infant of diabetic mother
- Inhibition of foetal parathyroids in maternal hyperparathyroidism
- Prolonged labour

Clinical Features

- Atrophy of skin and nails
- Bone—rickets (hypocalcaemic)/osteomalacia
- Carpopaedal spasm
- Convulsions
- Dental defects
- Decreased activity, lethargy
- Enamel defects
- Excitability of nervous system increased
- Growth retardation
- Hypoplasia of teeth
- Increased neuromuscular irritability
- Joint pains
- Jitteriness
- Laryngismus stridulus/stridor
- Manifest tetany—latent tetany can be tested by the tests given in Box 5.12

Investigations

- Serum calcium—low
- Electrocardiogram—prolonged QT interval

Treatment

- Calcium gluconate (10%) infusion is given at 2 mL/kg slowly by monitoring the heart rate. This is repeated every 6–8 hourly until the serum calcium becomes normal
- Correct alkalosis
- Treat the underlying conditions
- Vitamin D supplementation

BOX 5.12 Tests to demonstrate latent tetany

- *Trousseau's sign:* Blood pressure cuff is tied around the arm and the pressure is raised to above the systolic pressure. This is maintained for 3 minutes. This produces carpopaedal spam in presence of hypocalcaemia.
- *Chvostek sign:* The facial nerve is tapped where it emerges out of stylomastoid foramen. Twitching of orbicularis oris is seen in the upper lip or entire mouth.
- *Erb's sign:* Motor nerve stimulated electrically shows a positive response at a lower level of stimulus than the normal children.
- *Peroneal sign:* The peroneal nerve is tapped at a site on the head of the fibula where this nerve passes.

Hypercalcaemia

Causes are as follows:

- Hyperparathyroidism
- Excess of vitamin D intake
- Bone neoplasms
- Idiopathic hypercalcaemia

Clinical Features

- Anorexia
- Blood pressure increased
- Constipation
- Hypotonia
- Vomiting
- Heart block
- Renal stones
- Metastatic calcification in arteries, cornea, muscles and kidneys
- Mental changes

Treatment

- Decrease the intake of calcium
- Vitamin D
- Corticosteroids

Phosphorus

Bones contain 85% of the phosphorus. The remaining phosphorus is present in the cells. Phosphorus is absorbed from intestines, mainly jejunum. Kidneys play an important role in maintaining normal phosphorus levels. Phosphorus is filtered

in the glomerulus and reabsorbed in the tubules. Phosphates may be secreted in the distal tubules. Urinary excretion of phosphates is lowest in the morning and high in the evening.

Parathormone, vitamin D and growth hormone stimulate tubular reabsorption of phosphorus. Hyperphosphataemia occurs in hypoparathyroidism and renal failure. The absorption in the jejunum is decreased by thyrocalcitonin.

Hypophosphataemia

Hypophosphataemia occurs in starvation, protein energy malnutrition (PEM), malabsorption syndromes, prolonged intake of antacids (contain aluminium hydroxide which binds dietary phosphate).

Clinical Features

B	Bone pains
P	Pulp defects in the teeth
W	Weakness of muscles
A	Anorexia
R	Rickets (hypophosphatemic)
M	Malaise

Iodine

Iodine from the diet is absorbed by the small intestines and incorporated into thyroglobulin. It is a constituent of thyroxine (T_4) and tri-iodothyronine (T_3).

Deficiency

Predisposing factors for deficiency ar as follows:

- Excess calcium in the diet interferes with iodine absorption
- Goitrogens in the diet

Clinical Features

- Simple goitre—neck swelling
- Endemic cretinism—constipation, mental retardation, growth retardation, deafness, etc.

Treatment

- Diet rich in iodine
- Hypothyroidism should be treated with thyroxine

Selenium

Normal serum selenium level is 10–15 µg %. Its excess results in dental caries, alopecia, garlic odour in breath, etc.

Deficiency

Predisposing factors for deficiency are as follows:

- Protein energy malnutrition
- Total parenteral nutrition
- Poor soil content

Clinical features

- Growth retardation
- Liver necrosis
- Arthritis, myalgia
- Myopathy
- Keshan cardiomyopathy
- Increased incidence of cancers

Fluoride

Fluoride is a trace element. Common sources are drinking water (provides about 60% of daily requirement), seafoods, toothpastes and mouth rinses. Of these, fluoride from drinking water is the most assimilable form. Hence, excess levels in water are more toxic. The minimum and upper limits of fluoride levels recommended in the drinking water are given in Box 5.13. Fluoride consumption beyond the recommended levels predisposes to fluorosis.

BOX 5.13 Recommendations for fluoride levels in drinking water

Criteria	WHO recommendations	Indian Standard Code recommendations
Minimum fluoride levels (mg/L)	0.6	0.2
Upper limits of fluoride levels (mg/L)	1.5	1.0

REGULATORY FOODS

Regulatory foods include water and roughage. Roughage or dietary fibres have already been

discussed in the section *Carbohydrates* (page 174). Adequate roughage in the diet helps in normal bowel movements.

Water

Adequate water should be taken with food. Water is required in large quantities to regulate various functions of the body like digestion, excretion and maintenance of body temperature. Too little water results in poor digestion. Too much water results in poor assimilation. Recommended intake of water depends on the amount of calorie intake. Increased water should be taken in increased metabolic conditions like fever. The fluid requirement of the newborn is high due to increased urinary loss because of poor concentrating capacity of the kidneys. Also, the extracellular water content is more.

BALANCED DIET

A balanced diet is one that consists of all the food items like cereals, pulses and green vegetables in optimum proportions for that age and gender. A balanced diet should provide enough nutrients to facilitate the usual body functioning as well as reserve for stressful periods. ICMR recommendations for a balanced diet at various ages are given in Table 5.33. The following aspects should be considered while designing a balanced diet:

1. The calories derived from carbohydrates, proteins and fats should be in the following proportion:
   - Carbohydrates—55%–60%
   - Fats—30%–35%
   - Proteins—10%–15%
2. Carbohydrates should supply a major part of the calorie requirement in a normal diet. However, the energy derived from cereals should not be more than 75%. The calorie and protein content of some common food items is given in Table 5.34.
3. Protein ingestion has a negative effect on the appetite. So, the amount of protein intake should not exceed 15%–20% of the total calories required.
4. The ratio of proteins derived from cereals to that from pulses should be 4:1.
5. The minimum level of leafy and other vegetables should not be less than 150 g/day for an adult and proportionately for children (about 50 g). The green leafy vegetables supply vitamins A, C and B complex.
6. The minimum milk intake per day should be at least 100 mL in preschool children to 250 mL in adolescents and adults.
7. The energy derived from refined sugar or jaggery should be limited to about 5% of the total calorie intake. Excessive ingestion of refined sugars increases the risk of dental caries, causes hyperinsulinaemia and predisposes to hyperlipoproteinaemia and atherosclerosis. It

TABLE 5.33 Balanced Diet for Infants, Children and Adolescents (ICMR Recommendations)

Food Groups	g/portion	Infants (6–12 months)	Years						
			1–3	4–6	7–9	10–12		13–18	
						Girls	Boys	Girls	Boys
Cereals	30	1.5	4	7	9	9	11	10	14
Pulses	30	0.5	1	1.5	2	2	2	2	2
Milk (mL)	100	5	5	5	5	5	5	5	5
Roots and tubers	100	0.5	0.5	1	1	1	1	1	1
Green leafy vegetables	100	0.25	0.5	0.5	1	1	1	1	1
Other vegetables	100	0.25	0.5	0.5	1	1	1	1	1
Fruits	100	1	1	1	1	1	1	1	1
Sugar	5	5	5	6	6	6	7	6	7
Fats/oils	5	2	4	5	5	5	5	5	5

TABLE 5.34 Calorie and Protein Content of Common Food Items

Food Category	Food Stuff/ Preparation	Amount	Calories (kcal)	Protein (g)
Cereals	Rice (cooked)	100 g	325	7.5
	Wheat—chapatti	100 g	341	12.1
	Wheat—pooris	2	50–70	2
	Maize	100 g	340	11
	Barley	100 g	335	9.0–11.3
	Cornflour	100 g	360	8.6
	Idly	1	50	2
	Bread (white)	1 slice	50–70	2
	Dosa	1	50–70	2
	Upma	1 cup	250	6
	Ragi	100 g	330	7
Pulses	Cooked dal	1 tsp	10–15	0.5
	Soya bean	100 g	432	43.2
	Bengal gram powder	100 g	360	17
	Green gram	100 g	340	24
	Red gram	100 g	335	22.3
Leafy vegetables	Drumstick leaves	100 g	92	6
	Agathi	100 g	93	8
	Amaranth	100 g	45	4
	Spinach	100 g	26	2.0
	Cabbage	100 g	27	1.8
	Cauliflower	100 g	66	6
Other vegetables	Tomato	100 g	21	1.4
	Ladies finger	100 g	35	1.9
	Brinjal	100 g	24	1.4
Roots and tubers	Beetroot	100 g	43	1.7
	Carrot	100 g	48	0.9
	Potato	100 g	97	1.6
	Radish	100 g	17	0.7
	Sweet potato	100 g	12	1.2
Fruits	Apple	100 g	60	0.2
	Amla	100 g	0.5	0.6
	Orange	100 g	50	0.7
	Orange juice	100 mL	10	0.2
	Mango	100 g	44	0.7
	Banana (ripe)	100 g	116	1.2
	Papaya (ripe)	100 g	32	0.6
	Pineapple	100 g	46	0.4
	Pomegranate	100 g	65	1.6
	Raspberry	100 g	56	1.0
	Dates (dry)	10 g	317	2.5
	Guava	100 g	51	0.9
	Jackfruit	100 g	95	1.7
Milk and milk products	Breast milk	100 g	65	1.1
	Cow's milk	30 mL	20	1
	Butter milk	100 g	15	0.8
	Curd of cow's milk	100 g	60	3.1
Fats and oils	Butter	100 g	730	0
	Vegetable oil	100 g	900	0
Nuts	Coconut	100 g	444	4.5
	Almond	100 g	655	20
	Cashew nut	100 g	600	21
	Groundnut	100 g	560	27
Meat and poultry products	Egg (hen's)	1	66–80	6
		100 g	173	13.3
	Mutton	100 g	194	18.5
	Chicken	100 g	300	18
	Liver (goat)	100 g	107	20
	Beef	100 g	400	8
	Pork	100 g	114	18.7
Fish and sea foods	Fish	100 g	100–300	20–60
	Crab (muscle)	100 g	59	8.9
	Lobster	100 g	90	20.5
Miscellaneous	Biscuits	1	25	0.5
	Cane sugar	1 tsp	25	0

has also been associated with certain tumour growths like breast and colonic carcinoma.

8. Level of food items suggested should be consumable by an average child of same age.
9. The food should be palatable and should contain all the five basic tastes (sweet, salt, sour, bitter and umami) in acceptable proportions.
10. Adequate water should be consumed. Too much water interferes with digestion whereas too little water compromises assimilation.
11. The economic, cultural and geographic constraints should be taken into consideration. The food items suggested should be affordable, acceptable and available.

MULTIPURPOSE FOOD

It is recommended to prevent malnutrition in children. It provides a balanced diet and meets the requirements of the child. This diet can also be given to malnourished children.

Staple foods (40 g)	Protein supplements (15 g)	Vitamin and minerals	Energy supplements
Rice Wheat	Beans Groundnuts Fish Egg	Green leafy vegetables Fruits	Vegetable oils Ghee Sugar

Multimix Foods

These are mixtures which are rich in protein and energy and advised for treatment of PEM at home. These supply adequate calories and proteins to the child. Each 100 g contains ragi (40 g), wheat (35 g), Bengal gram roasted (15 g) and groundnuts (10 g). These supply about 500 kcal and 15 g of protein.

Hyderabad Mixture

The National Institute of Nutrition at Hyderabad has recommended a mixture which is rich in calories and proteins. Each 86 g of this mixture supplies 330 calories and 11.5 g of protein. The constituents are

- Whole wheat (40 g)
- Bengal gram (16 g)
- Groundnut (10 g)
- Jaggery (20 g)

MALNUTRITION

The term *malnutrition* is used to denote undernutrition, overnutrition and selective nutritional deficiencies. However, the terms malnutrition, PEM and undernutrition are often used interchangeably. Undernutrition occurs due to inadequate intake, poor absorption or excessive loss of nutrients. Overnutrition occurs due to excessive intake of nutrients.

PEM is defined as a range of pathological conditions arising from coincident lack of proteins and calories in varying proportions in infants and young children. It is commonly associated with infections. It is one of the major causes of death in children below 5 years of age.

CAUSES OF UNDERNUTRITION

1. Primary causes—lack of adequate intake of food
   - Poverty—inability to spend money on food in order to fulfil nutritional requirements
   - Ignorance—lack of awareness of the nutritional qualities of food
   - Food fads—reservations for eating specific foods
   - Traditional habits—continuation of breast milk without introduction of complementary feeding at appropriate age, use of over-diluted food formulas and restriction of food intake during periods of certain illness like diarrhoea
   - Social and cultural factors—males are given more food than females
   - Congenital defects like cleft palate and cleft lip, which interfere with food intake
   - Intrauterine growth retardation (IUGR) and maternal malnutrition predispose child to undernutrition later in life
2. Secondary causes—undernutrition occurs despite adequate intake of food
   - Chronic illness and infections (Box 5.14)—increased metabolic needs and lack of appetite
   - Malabsorption/impaired utilisation
   - Excessive loss—gastroenteritis
   - Drugs—INH predisposes to pyridoxine deficiency, phenytoin predisposes to folic acid deficiency

INDICATORS OF PEM

The children with PEM are classified based on various indicators to describe the duration and severity of undernutrition. These indicators are

BOX 5.14 Illness and infections predisposing to undernutrition

- Infections—tuberculosis, human immunodeficiency virus (HIV), chronic diarrhoea, pneumonia.
- Metabolic diseases—inborn errors of metabolism.
- Gastrointestinal tract—cleft lip, cleft palate, malabsorption, gastro-oesophageal reflex.
- Liver—chronic liver disease, hepatitis.
- Pancreas—pancreatic insufficiency.
- Renal—urinary tract infections, chronic renal failure, renal tubular acidosis.
- Respiratory causes—asthma, recurrent respiratory tract infections.
- Endocrine causes—diabetes mellitus, hypothyroidism, Addison's disease, growth hormone deficiency.
- Neurological causes—mental retardation, degenerative diseases, cerebral palsy (palatopharyngeal in coordinations which results in swallowing problems and thereby decreased intake).
- Collagen vascular diseases.
- Malignancies.

- weight for age (W/A),
- height for age (H/A) and
- weight for height (W/H).

Calculation and Interpretation of Indices

These indicators are useful in differentiating acute from chronic malnutrition. In acute malnutrition, the child has low weight for age but the height for age is normal. In chronic malnutrition, both the weight for age and height for age are low, but the weight for height is normal as both weight and height are decreased (Table 5.35).

Weight for Age

$$\text{Weight for age} = \frac{\text{Weight of the child}}{\text{Weight of normal child of same age}} \times 100$$

TABLE 5.35 Interpretation of Indicators

Indicator	Acute Malnutrition	Chronic Malnutrition
W/A (underweight)	Low	Low
H/A (stunting)	Normal	Low
W/H (wasting)	Low	Normal

This is the most sensitive indicator for malnutrition. If the child has low weight for age, he/she is said to be underweight. Low weight for age is seen in both acute and chronic malnutrition.

Height for Age

$$\text{Height for age} = \frac{\text{Length/height of the child}}{\text{Length or height of normal child of same age}} \times 100$$

If the child has low height for age, he/she is said to be stunted. It implies chronic malnutrition. However, this indicator should be interpreted carefully as many diseases and syndromes are associated with short stature.

Weight for Height

$$\text{Weight for height} = \frac{\text{Weight of the child}}{\text{Weight of normal child of same height}} \times 100$$

If a child has low weight for height, he/she is said to be wasted. Low weight for height implies acute malnutrition.

CLASSIFICATION OF PEM

On the basis of the indicators, as explained above, the undernourished children are classified into various grades by different classification schemes.

IAP Classification (1972)

The National Subcommittee of the Indian Academy of Paediatrics has accepted the standard value (100%) as 50th percentile of Harvard Standard. This classifies PEM into four grades as follows:

Nutritional status	Weight for age (%) of 50th percentile of Harvard standard
Normal	>80
Grade I PEM	71–80
Grade II PEM	61–70
Grade III PEM	51–60
Grade IV PEM	<50

If there is nutritional oedema, a letter K should be placed along with the grade of PEM.

Wellcome Trust Classification (1970)

It is based on weight for age values and the presence or absence of oedema. The disadvantage of Wellcome classification is that it takes no account of stunting and hence the duration of malnutrition.

Weight for age (Boston) (% of expected)	Oedema present	Oedema absent
60%–80% of standard	Kwashiorkor	Undernutrition
<60% of standard	Marasmic kwashiorkor	Marasmus

Jellife Classification (1965)

It classifies malnutrition into four degrees according to weight for age.

Nutritional status	Weight for age (%) of 50th percentile of Harvard standard
Normal	>90
I degree PEM	80–90
II degree PEM	70–79
III degree PEM	60–69
IV degree PEM	<60

The disadvantage of this scoring system is that it takes weight for age below 90% as malnutrition. In developing countries, most of the children are considered as malnourished according to this grading. Hence, the classifications in India consider any child above 80% as normal.

Gomez Classification (1956)

It is the earliest system of classification of children with malnutrition according to weight for age. It is based on the percentage of expected weight for age according to Harvard standard. This classifies malnutrition into three degrees.

Nutritional status	Weight for age (% of expected) (50th percentile of Harvard standard)
Normal	>90
I degree PEM (mild)	76–90
II degree PEM (moderate)	60–75
III degree PEM (severe)	<60

If the child has oedema, it should be classified as III degree PEM, as suggested by Bengoa in 1977. Disadvantage of Gomez classification is that it uses an external standard of Harvard. Also, like Jellife classification, children below 90% are considered as malnourished.

WHO Classification

It is based on weight for height (wasting), height for age (stunting) and presence of oedema. The WHO recommends the use of *Z* scores or standard deviation (SD) scores to indicate how far away the child's measurement falls from the median (*Z* score = 0). The calculations are based on the *Z*-score percentile charts developed by the WHO.

Parameters	Moderate undernutrition	Severe undernutrition
Symmetrical oedema	Absent	Present (oedematous malnutrition)[a]
Weight for height (measure of wasting)	*Z* score or SD score[b] between −2 and −3 (70%–79% of expected) Wasting	*Z* score or SD score <−3 (70% of expected) Severe wasting
Height for age (measure of stunting)	*Z* score or SD score between −2 and −3 (85%–89% of expected) Stunting	*Z* score or SD score <−3 (<85% of expected) Severe stunting

[a]Includes kwashiorkor and marasmic kwashiorkor.

[b]SD score or *Z* score = $\frac{\text{Observed value} - \text{median reference value}}{\text{Standard deviation of reference population}}$

McLaren Classification

This is based on height for age.

Classification	Height for age (% of expected)
Normal	93–105
Short	80–93
Dwarf	<80

Classification based on NCHS Standards

National Centre for Health Statistics (NCHS) had suggested the following classification in the United States:

Indices	Nomenclature	Cutoff points for defining malnutrition	
		% of reference median	*Z* or SD score from reference median
Weight for height	Wasting	<80	< −2
Height for age	Stunting	>90	< −2
Weight for age	Underweight	<80	< −2

Waterlow Classification (1972)

Waterlow has suggested a classification of populations in tabulation to combine the effects of chronic PEM on weight for height and height for age. The classification is based on the degree of wasting and stunting. This helps in identifying acute and chronic malnutrition.

Waterlow Classification based on height for age

Classification	Height for age (% of expected)
Normal	>95
First-degree stunting	90–95
Second-degree stunting	85–89
Third-degree stunting	<85

Waterlow Classification based on weight for height

Classification	Weight for height (% of expected)
Normal	>90
Mild wasting	80–90
Moderate wasting	70–79
Severe wasting	<70

Waterlow classification is helpful in guiding interventions of a malnourished child but does not indicate when, how and why the stunting or wasting has occurred. Stunted children do not need urgent intervention as the condition cannot be reversed whereas wasted children need urgent intervention as the mortality is high. Different priorities of action could be taken, though it can also serve in monitoring the group.

Action intervention in malnutrition

Group	Assignment
Wasted and stunted	Priority in action
Wasted but not stunted	Action
Not wasted but stunted	Action depending upon the resources
Not wasted and not stunted	No action
Weight above 120% of the reference weight (obesity)	Action to reduce weight

Classification Suggested by FAO/WHO Expert Committee on Nutrition

The first health assembly suggested that the Joint FAO/WHO Expert Committee on nutrition classify the children with protein calorie malnutrition. The Eighth Joint Expert Committee on Nutrition of FAO and WHO emphasised the need for an accepted classification and definition of protein calorie malnutrition. A qualitative classification is helpful in assessing the different patterns of children with malnutrition whereas a quantitative classification is helpful in community studies of prevalence and severity. The prevailing pattern of malnutrition in an area gives information about the nature of dietary deficiency. This guides about the preventive measures that can be taken in the community (Table 5.36).

Age-Independent Criteria

The lack of knowledge of the accurate age of children makes it difficult to suspect malnutrition in the early stages. Age-independent criteria are used in such children to assess the nutritional status. These criteria do not vary with age and remain constant irrespective of the age.

TABLE 5.36 Classification Suggested by FAO/WHO Expert Committee on Nutrition

Nutritional Status	Body Weight (% Standard) for Age	Oedema	Deficit in Weight for Height
Underweight	80–60	0	Minimal
Nutritional dwarfism	60	0	Minimal
Marasmus	<60	0	++
Kwashiorkor	80–60	+/++	+/++
Marasmic kwashiorkor	<60	+	++

- Midarm circumference (1–5 years)
- Weight for height
- Skinfold thickness (1–6 years)
- Enderberg index
- Kanawati index
- Rao and Singh's index
- Dugdale's index
- Midarm circumference/height ratio
- Ponderal index
- Quetelet index
- Body mass index
- Chest/head circumference ratio

Midarm Circumference

Midarm circumference is constant between 1 and 5 years of age. The circumference is around 16–17 cm. MAC is measured with a measuring tape. PEM can be classified on the basis of MAC as follows.

Arnold's Classification. Arnold's classification of PEM is based on MAC of the child. The disadvantage in using this system of classification is that in oedematous child, the value may be wrong (as in cases of kwashiorkor) (Table 5.37).

Bangle Test. The child's arm is inserted into a bangle with an inner diameter of 4 cm. This is done in children below 5 years of age. If the bangles cross the elbow, it indicates that the MAC is decreased. In normal children, the bangle cannot pass above the elbow.

TABLE 5.37 Arnold's Classification

Grades	Midarm Circumference (cm)
Normal	16
Mild PEM	Between 13.5 and 16
Moderate PEM	Between 12.5 and 13.5
Severe PEM	< 12.4

TABLE 5.38 Colour Coding in Shakir's Tape and Corresponding MAC

MAC	Colour	Inference
>13.5	Green	Normal
12.5–13.5 cm	Yellow	Borderline
<12.5 cm	Red	Wasted

Shakir's Tape. This tape has three zones with the colours red, yellow and green. The tape is placed over the midarm to see in which zone the MAC falls. This is a simple and easy way to assess the presence of malnutrition (Table 5.38).

Quac–Stick Method. The Quaker stick is a height measuring rod which also shows the expected normal MAC for that height. Measure both the MAC and the height of the child. Now calculate the expected height for the MAC. Place the stick by the side of the child, with the child standing in erect posture. If the height of the child is more than that expected for his MAC, it indicates that the child is having a MAC lower than the expected. This indicates muscle wasting and presence of malnutrition. The child should be evaluated further.

Modified Quac–Stick Method. It uses the colours green, yellow and red to indicate malnutrition as in Shakir's tape. In Shakir's tape, only MAC is measured. In modified Quac–Stick method, both MAC and the height are measured. The expected height for the MAC is calculated and verified.

Weight for Height

In children with acute malnutrition, the weight is decreased but the height is not affected. In such children, the weight for height is less. But in children with chronic malnutrition, both the height and weight are decreased. In these children, the weight for height is normal.

$$\text{Weight of child (kg)} = \frac{\text{Percentage weight for height}}{\text{Weight of normal child of same height (kg)}} \times 100$$

This is decreased in acute malnutrition, but normal in chronic malnutrition as both height and weight are decreased for age.

Skinfold Thickness

This indicates the status of fat deposits in the body. The skinfold thickness is measured at biceps, triceps, infrascapular and suprailiac regions. Harpenden caliper is used to measure the skinfold thickness.

The triceps skinfold is measured midway between the acromion and olecranon process in the left arm. The skinfold should be measured in the vertical plane with the arm hanging in a relaxed manner by the side of the body.

Subscapular skinfold thickness is measured at the inferior angle of scapula. The skin is pinched just below the angle of scapula.

For measuring biceps' skinfold thickness, the skin is pinched over the belly of the biceps at a point midway between the antecubital fossa and the head of the humerus.

Adequate pressure should be maintained while taking the measurements. This is important as high pressure results in falsely low values, while low pressure gives abnormally high values. Pressure should be maintained at 10 g/mm^2.

The normal value is more than 10 mm in children between 1 and 6 years. Skinfold thickness <6 mm is abnormal and indicates severe malnutrition.

Enderberg Index

This index is age-independent only up to 13 years and is calculated as follows:

$$C = \text{Log (weight in kg)} - 1.6 \text{ (height in cm)}$$

Normal value of C is 40. C denotes the Enderberg index. This remains constant up to 13 years of age.

Kanawati Index

It is the ratio between the MAC and head circumference.

$$\text{Kanawati index} = \frac{\text{MAC (cm)}}{\text{Head circumference (cm)}}.$$

This ratio remains a constant for children between 4 months and 4 years of age irrespective of sex. The normal value is more than 0.32.

The malnutrition can be graded according to the values of the index as follows:

Grade of malnutrition	Kanawati Index
Mild malnutrition	0.28–0.32
Moderate malnutrition	0.25–0.28
Severe malnutrition	<0.25

Rao and Singh's Index

It is calculated as

$$\frac{\text{Weight (kg)}}{(\text{Height in cm})^2} \times 100.$$

Normal value is 0.15–0.16. In PEM, the value lies between 0.12 and 0.14. Normal value 0.15 is constant for growth up to 5 years. Since it depends on the body mass, any change indicates malnutrition.

Dugdale's Index

This index value is calculated as

$$\frac{\text{Weight of the child (kg)}}{(\text{Height in cm})^{1.6}} \times 100.$$

The expected normal value is 0.88–0.97. It is less than 0.79 in malnutrition.

MAC/Height Ratio

This is calculated by dividing MAC by the height of the child.

$$\text{MAC/height ratio} = \frac{\text{MAC (cm)}}{\text{Height (cm)}}$$

Normal value is 0.32–0.33. Value less than 0.29 indicates gross malnutrition.

Ponderal Index

$$\text{Ponderal index} = \frac{\text{Weight (g)}}{\text{Height (cm)}^3} \times 100$$

It is less than 2 in severe protein energy malnutrition.

Ponderal Index	Significance
>2.5	Normal
2–2.5	Borderline PEM
<2	Severe PEM

Significance of PI in Newborn Babies. PI greater than 2.5 is seen in term and appropriate-for-date babies and is less than 2 in babies with asymmetrical IUGR.

Ponderal Index	Significance in newborn
>2.5	Term, appropriate for date baby
<2	Asymmetrical IUGR
>2	Symmetrical IUGR

Body Mass Index

Body mass index (BMI) is expressed as the ratio between weight (kg) and height $(m)^2$. It is calculated as

$$\text{BMI} = \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}.$$

Nutritional intervention is needed if the BMI is less than 15 or less than 5th percentile in children and adolescents.

Quetelet Index

It is calculated as

$$\frac{\text{Weight (kg)}}{[\text{Height (cm)}]^2} \times 100.$$

Normal value lies between 0.14 and 0.16. In malnutrition, it is below 0.14. Note that this is similar to BMI but the values there are in SI units.

Chest/Head Circumference Ratio

It is calculated as

$$\frac{\text{Chest circumference}}{\text{Head circumference}}.$$

The ratio is less than 1 in children below 1 year of age. At 1 year of age, the head circumference is equal to chest circumference so that the ratio equals 1. The ratio is more than 1 after 1 year of age in normal children but in PEM, the ratio is less than 1 even after 2 years of age.

PATHOGENESIS

Gopalan's Theory of Adaptation

Some children develop marasmus while others develop kwashiorkor even though there is no quantitative and qualitative difference in their diets. This is explained by the Gopalan's theory which says that marasmus develops due to good adaptation to poor diet while kwashiorkor is the result of adaptation failure.

In marasmus, decreased calorie intake leads to decreased insulin levels and increased cortisol levels. Increased cortisol level leads to tissue catabolism, which causes muscle wasting. In this process, glucose and amino acids are released into the circulation. The glucose is utilised by the brain and the amino acids are used for synthesis of albumin and β-lipoprotein. Thus, the albumin level is maintained in the blood and hence no oedema occurs in marasmus. The β-lipoprotein helps in mobilising the fat from the liver; hence, the fat is not accumulated in the liver.

In kwashiorkor, there is increase in insulin level which prevents tissue catabolism. Hence, the amino acids are not available for albumin synthesis and β-lipoproteins are not formed. Hence, oedema and fatty liver develop.

Golden's Theory of Free Radicals

In PEM, free radicals play a role in the pathogenesis of oedema. According to Golden's theory, antioxidant depletion may cause kwashiorkor and it may, therefore, be prevented with antioxidant supplementation.

PATHOLOGICAL AND BIOCHEMICAL CHANGES IN PEM

PEM affects almost all the systems. Various pathological changes that occur are summarised in Table 5.39. Table 5.40 lists the important biochemical changes that occur in the body.

MARASMUS

Marasmus is the commonest type of severe PEM that occurs in preschool children and results in growth retardation and muscle wasting without oedema.

TABLE 5.39 Pathological Changes in PEM

Organ/System	Pathological Changes
Cardiovascular system	Microcardia—reduced myocardial mass, atrophy and patchy necrosis of myocardium Cardiomegaly in thiamine or selenium deficiency, anaemia, cardiac failure, cardiomyopathy, pericardial effusion
Respiratory system	Atrophy of intercostal muscles
Gastrointestinal tract	Mucosal atrophy, delayed mucosal repair, atrophy of intestinal villi (malabsorption) Reduced gastrointestinal enzyme secretions
Liver	Fatty change (fatty infiltration) starts from the periphery of the lobule and extends towards the centre
Endocrine system	Generalised atrophy Insulin levels are decreased Thyroid hormone levels are decreased Growth hormone level is increased Cortisol level is increased
Immunological system	Severe malnutrition leads to impaired immunity Non-specific immunity due to mucosal skin barrier, chemotaxis, lysozymes, complements, interferon, interleukin II, etc. is defective Cell-mediated immunity will be low Humoral immunity is more or less maintained but antibody production to diphtheria is low. Also, secretory IgA will be low which predisposes to respiratory and gastrointestinal infections Impaired T and B lymphocyte functions Decreased lymphocyte count Delayed skin hypersensitivity
Hair	More evident at the root of the hair Change in texture Hypopigmented
Others	Impaired functioning of all organs Malnutrition leads to delayed wound healing

Predisposing Factors

- Early abrupt weaning
- Intake of diet with inadequate calories and protein
- Infections—gastroenteritis
- Malabsorption disorders

TABLE 5.40 Biochemical Changes in PEM

Parameter	Biochemical Changes
Proteins	Reversal of albumin-globulin ratio—albumin decreased, γ-globulins increased, β-globulins decreased (α-1 globulin may be increased; α-2 globulin low) Serum amino acid pattern altered—reversal of non-essential/essential amino acid ratio in PEM >3.5 (normal 1.5) All enzymes—low Amino acid pool—decreased Serum β-lipoproteins decreased Serum transferring decreased (<0.45 mg/dL)
Carbohydrates	Depletion of glycogen reserves in the liver and muscle Blood sugar is low
Lipids	EFA decreased Non-EFA to EFA ratio increases above 3 Fatty liver in kwashiorkor Serum lipids normal or high
Electrolytes	Sodium is normal or increased; hyponatraemia in dilutional hyponatraemia Potassium decreases
Water	Total body water increases High extracellular fluid/intracellular fluid ratio
Minerals and trace elements	Iron, zinc, manganese, copper, calcium, phosphorus, magnesium and potassium decreased

Pathogenesis

A diet which is deficient in both calories and proteins leads to decreased insulin and increased cortisol levels in the plasma. This leads to the following effects:

- Mobilisation of protein from the muscle and subcutaneous tissue—this leads to muscle wasting. It is often said that a marasmic child lives on his own flesh.
- Decreased levels of growth hormone due to raised cortisol levels—this leads to growth retardation.
- The body's amino acid levels are maintained due to mobilisation of proteins and are available for hepatic synthesis of albumin. Hence, there is no oedema.
- The β-lipoproteins remove the fat from liver, so there is no fatty liver, as in kwashiorkor.

Clinical Features

Salient features of marasmus are as follows:

- Weight—decreased <60% of the expected.
- Muscle wasting—can be seen best at the temporalis and scapular muscles. Measurement of MAC also indicates muscle wasting.
- Growth retardation—marked stunting.
- Loss of subcutaneous fat—leads to old-man appearance. Loose folds of skin can be seen over the glutei and inner side of thigh (Fig. 5.6).

Head-to-Toe Examination

1. Appearance
   - Old-man appearance
   - Cry is good
2. Head
   - Microcephaly
   - Delayed closure of anterior fontanel



FIGURE 5.6 A marasmic child with old-man appearance, severe muscle wasting and skin lesions. Note the loose folds of skin over the inner side of thigh.

3. Neck
   - May appear long due to loss of subcutaneous fat and muscle wasting
4. Abdomen
   - Scaphoid
   - Abdominal distension can be seen, due to diarrhoea causing hypokalaemia and decreased muscle tone
5. Extremities
   - Thin due to wasting

Grading

The children are assessed for malnutrition on the basis of history and examination findings. They can be graded for severity of PEM according to the weight and height. Total dietary recall is done and calorie gap and protein gap should be assessed. On the basis of the loss of fat at different places in the body, marasmus can be graded as given in Table 5.41. Loss of fat is first seen in axilla and groin.

TABLE 5.41 Grading of Marasmus

Grades	Area of Loss of Fat
I	Axilla/groin
II	Grade I + thigh/buttocks
III	Grade II + chest/abdomen
IV	Grade III + buccal pad of fat

Complications

- Hypoglycaemia
- Hypothermia
- Infections
- Electrolyte imbalances
- Growth retardation (both physical and mental)
- Behaviour changes
- Poor school performance
- Motor coordination affected
- Intelligence affected

Investigations

- Complete blood count
- Serum proteins
- Peripheral smear
- Blood sugar
- Serum electrolytes
- Urine routine and microscopic examination
- Stool routine and microscopic examination
- Investigations to find out associated infections—urine culture, blood culture, Mantoux test, chest X-ray

Treatment

Most of the children respond well to oral diet rich in calories and proteins as the appetite is good. Children who are severely malnourished need to be admitted in the hospital as there is atrophy of the intestinal epithelium and the exocrine pancreas. Food must be started in small quantities. The weight should be monitored.

- Diet should be affordable/acceptable/available. Calorie requirement is 150–200 kcal/kg/day for the present weight. Protein requirement is 2–3 g/kg/day for the present weight. The calories can also be calculated for the expected weight for present age. The RDA for the expected weight for age can be given. Step up the calorie intake if needed. Improve the calorie content of the food by adding sugar or oil. Make the food isodense so that 100 mL of food will provide 100 kcal.
- Parenteral nutrition can be given if the child is not tolerating oral feeds or in any condition where oral feeds are contraindicated. Partial parenteral nutrition provides a part of the required calories parenterally. Total parenteral nutrition provides the total required calories parenterally.
- Vitamin supplementation—vitamin A deficiency is not common in marasmus unlike kwashiorkor. If present, it should be treated. Folic acid supplementation is done.
- Mineral supplementation—iron is started after 3 months. Electrolyte imbalance should be corrected, if present.
- Treatment of associated infections.
- Treatment of worm infestations.
- Treatment of complications (see section *Treatment*, page 217).

Rehabilitation and Follow-up

Rehabilitation is done by health education and registration in nutritional clinic. The weight of the

child is monitored frequently during follow-up. If there is no adequate weight gain or there is weight loss in spite of adequate calories and protein, other causes of failure to thrive should be searched for. The child should also be investigated for presence of infections.

Catch-up Growth

The growth rate is slow when the food intake is decreased. The body weight is affected most followed by the body length. Once the calorie and protein intake are restored, the growth velocity increases up to 4 times above the normal for the age. The catch-up growth never exceeds the predetermined rates of growth. The control mechanism for the catch-up growth diminishes as the catch-up growth approaches the target growth.

Prognosis

As there are no life-threatening complications, the prognosis is good in marasmic children. Once the child develops oedema (marasmic kwashiorkor), the treatment becomes difficult.

KWASHIORKOR

The term 'kwashiorkor' means the influence on the older child when the next baby is born. It is protein deficiency malnutrition and commonly occurs in children who are weaned from mother's breasts to a diet rich in starch and low in proteins. It is characterised by three essential clinical features:

- Retarded growth
- Psychomotor changes
- Oedema

Kwashiorkor occurs from early infancy to 5 years of age. It is most commonly seen in the second year of life.

Clinical Features

Changes should be identified in the early stages only and treated accordingly. One should not wait for the typical changes to occur, which may be seen only in florid kwashiorkor.

Features Usually Present

1. Growth retardation
   - Decreased weight—60%–80% of the expected weight
   - Stunting—decreased height
2. Oedema—generalised, pitting, fast oedema.
3. Behavioural changes
   - Irritability (Fig. 5.7a)
   - Anorexia
   - Listlessness
   - Lethargy
   - Apathy
   - Cry—moaning
   - Resents handling
   - Lack of interest in surroundings
4. Hair changes—more evident at the root of the hair in the early stages of acute PEM. These include hair that are hypopigmented (blond hair, reddish or grey), thin, dry, brittle, lustreless, sparse and easily pluckable. Flag sign is usually positive, that is, the pigmentation of hair is alternately normal and depigmented (Fig. 5.8). There are associated changes in texture and straightening of curly hair
5. Skin changes—these are commonly seen on the areas exposed to continuous pressure and irritation (Fig. 5.7b)
   - Bullous lesions
   - Bleeding—purpura, petechiae and ecchymoses in severe cases
   - Dermatosis—it may be crazy pavement dermatosis/paddy field dermatosis/flaky paint (enamel paint) dermatosis. Various changes are seen together in mosaic-type dermatosis.
   - Erythema
   - Flexural ulcers
   - Gangrenous lesions
   - Hyper/hypopigmentation—the areas of hyperpigmentation desquamate exposing the hypopigmented area
   - Mucocutaneous lesions—smooth tongue and stomatitis
   - Infections—secondary skin infection may occur



(a)



(b)

FIGURE 5.7 Kwashiorkor. (a) Oedematous and irritable child with thin hypopigmented and sparse hair. (b) Child has generalised oedema, irritability and typical skin changes—flaky paint dermatoses.



FIGURE 5.8 Flag sign in kwashiorkor: The hair show alternating black and white areas.

6. Muscular changes
   - Muscle wasting—can be seen in the shoulders and upper arms. The presence of oedema may mask the muscle wasting.
   - Hypotonia—due to hypokalaemia and muscle wasting
   - Hypertonia—due to hypomagnesaemia and hypocalcaemia

Features Occasionally Present

- Hepatomegaly due to fatty infiltration
- Associated vitamin deficiencies like vitamin A deficiency
- Pot belly due to hypotonia and weakness of the abdominal muscles

Associated Problems

- Diarrhoea
- Respiratory infections
- Urinary tract infections
- Vitamin deficiency symptoms—vitamin A, thiamine, riboflavin and niacin deficiencies

Aetiology of Various Clinical Features

Oedema

The factors that play an important role in the pathogenesis of oedema in a child with malnutrition are given below:

Decreased factors	Increased factors
Albumin	Aldosterone
Potassium	Antidiuretic hormone
Haemoglobin (anaemia)	Free radical
Cardiac function	Ferritin
Vanadium	Rennin
Zinc	Insulin
	Cortisol (plasma)
	Angiotensin

Hair Changes

Hair changes are due to

- Protein deficiency
- Relative zinc deficiency
- Tyrosine deficiency
- Copper deficiency
- Low levels of cysteine
- Low levels of melanin

Skin Changes

- Alteration in the hydroxy proline and proline

ratio due to low protein intake
- Tyrosine deficiency
- Melanin deficiency
- Vitamin deficiencies—niacin, vitamins C and K deficiency
- Zinc deficiency
- Gram-negative septicaemia and disseminated intravascular coagulation; predispose to purpura and bleeding

CNS Changes

Mental changes in kwashiorkor are due to

- Alteration in neurotransmitter synthesis and release
- Brain oedema
- Calories decreased
- Degenerative changes and reduction in dendritic arborisation
- Electrolyte imbalances such as hypokalaemia and hypomagnesaemia

Muscular Changes

- Hypotonia—reduced potassium in the blood and nutritional myopathy
- Hypertonia—reduced calcium or magnesium levels in the blood

Cardiac Changes

- CCF (cardiomegaly)
- Anaemia
- CCF (Nutritional recovery syndrome)
- Pericardial effusion (due to hypoproteinaemia)

Grading

Children with kwashiorkor can be graded, as shown in Table 5.42, on the basis of presence of oedema at different sites. Grade I carries a better prognosis. Grades III and IV require urgent intervention.

TABLE 5.42 Grading of Kwashiorkor

Grades	Clinical Findings
I	Pedal oedema
II	Grade I + facial oedema
III	Grade II + paraspinal and chest oedema
IV	Grade III + ascites

Investigations

In kwashiorkor, the diagnosis is mainly clinical and based on anthropometry. Investigations are done to find out associated problems.

1. To find out the associated infections
   - Blood culture (for sepsis)
   - Peripheral smear for malaria
   - Stool examination for ova/cyst
   - Sputum examination or resting gastric juice examination for acid-fast bacilli of tuberculosis
2. To find out the complications
   - Blood sugar (hypoglycaemia)
   - Serum electrolytes (hypokalaemia, hypernatraemia or dilutional hyponatraemia)
   - Chest X-ray (heart failure, bronchopneumonia)
   - ECG (heart failure)

Complications

- Hypothermia
- Hypoglycaemia
- Hypokalaemia
- Hyponatraemia (dilutional) or hypernatraemia
- Heart failure
- Infections—bronchopneumonia/oral thrush
- Dehydration

Treatment

Children with kwashiorkor can not tolerate the feeds with required calories and proteins if given all of a sudden. Hence, the feeding should be started with decreased amount of calories and then gradually increased over a period of 1 or 2 weeks.

The first intention of the management should be to save the child. So, one need not expect the child to grow during this period. So, 12.5% of calories needed for growth can be avoided. Twenty-five per cent of calories required for daily activity can also be avoided by putting the child on bed rest. Hence, if the child's requirement is 1000 cal, start with only 62.5% of this; that is 625 cal (approximately two-thirds of the requirement of existing weight irrespective of oedema). Calorie intake should be

increased gradually. Start with foods which supply 80–100 kcal/kg/day and 1–1.5 g/kg of protein per day for the existing weight (0.7 g/kg/day in very sick child). Gradually, increase this to 150–200 kcal/kg for the existing weight within a week. Calorie intake should be increased more slowly in severe cases.

The goal is to provide calories 150–200 kcal/kg/day of existing weight irrespective of oedema, protein 3–4 g/kg/day and fluid 100–165 mL/kg/day. In few children, about 150% of the RDA can be given to the children with malnutrition. A total of 10%–15% of the required calories should be given as oil. Coconut oil is rich in medium-chain triglycerides and can be given.

Prevention and treatment of complications is discussed in the section *Treatment*, page 217.

Manifestations of Recovery

Recovery in response to management may be assessed by improvement in clinical and biochemical parameters. Clinical parameters are as follows:

1. Appetite improved
2. Weight gain—in kwashiorkor, the weight is lost initially due to loss of fluid. The oedema usually disappears within 7–10 days. Child reaches normal weight by 6–8 weeks.
   - Good weight gain is said to be present if the weight gain is at least 10 g/kg/day.
   - Moderate weight gain is said to be present if the weight gain is at least 5–10 g/kg/day.
   - Poor weight gain is said to be present if the weight gain is <5 g/kg/day.
3. Increased motor activity—child shows interest in surroundings and becomes playful.

Table 5.43 lists the clinical responses seen in a child on treatment according to the day of treatment.

TABLE 5.43 Timeframe for Response to Treatment in a Child with Kwashiorkor

Response of the Child	Day of Treatment
Return of social smile	3–4 days
Appetite	4–5 days
Skin changes	3–4 weeks
Hair changes	3–6 months
Bitot's spots	Long time to disappear

Biochemical improvement is suggested by a rise in serum albumin levels.

Rehabilitation

- Registration in nutrition clinic
- Nutritional counselling
- Follow-up
- Vocational therapy

Prognosis

The prognosis is poor in the presence of the following factors:

- Associated infections—septicaemia, pneumonia, etc.
- Shock
- Dehydration
- Severe anaemia
- Electrolyte disturbances
- Vitamin deficiencies
- Serum albumin levels—less than 1.5 mg/dL
- Purpura/purpuric spots
- Hypothermia
- Hypoglycaemia
- Massive oedema
- Mental apathy
- Hepatomegaly

Long-term prognosis depends on

- Per capita income
- Literacy levels
- Environmental conditions
- Available healthcare facilities
- Size of the family

MARASMIC KWASHIORKOR

This condition is associated with features of both marasmus and kwashiorkor.

The child is said to have this condition when all of the following features are present:

- Weight <60% of the expected weight
- Oedema
- Marked wasting and stunting
- Anaemia
- Mental apathy

Wasting is more obvious in the upper part of the body and oedema in the lower part of the body. Skin and hair changes associated with kwashiorkor may be seen.

PREKWASHIORKOR

This is a condition which is seen before a child with malnutrition develops kwashiorkor. Features are as follows:

- Poor weight gain
- Behaviour changes
- Loss of fat from subcutaneous tissue
- Early hair changes
- Skin changes—may be seen
- Hepatomegaly
- Oedema in the lower part of the body

FLORID KWASHIORKOR

This is the most severe form of kwashiorkor with typical features of kwashiorkor. The onset is rapid with oedema, muscle wasting, skin changes and mental changes. Differences between marasmus and kwashiorkor are summarised in Table 5.44.

MANAGEMENT OF PEM

Management of PEM includes the following:

- Nutritional assessment
- Investigations
- Treatment

NUTRITIONAL ASSESSMENT

The growth and development of a child depends upon the nutritional status of the child. Special care should be given to children with malnutrition. For this purpose, the children should be assessed for nutritional status (Table 5.45). This helps in identifying children who need special care.

Clinical Assessment

It is done by noting the anthropometry and the clinical features of malnutrition. Wasting, oedema

TABLE 5.44 Differences between Marasmus and Kwashiorkor

Features	Marasmus	Kwashiorkor
Aetiology	Decreased intake of both proteins and calories and other nutrients	Decreased protein intake
Age	Common below 1 year (0–3 years)	1–4 years
Incidence	More common	Less common
History		
Appetite	Good	Anorexia
Complementary feeding (weaning)	Early	Late
Clinical examination		
Appearance	Old man appearance	Moon face
Sensorium/activity	Alert, playful, active/apathetic	Apathy, dull, irritable
Weight	Less than 60%	60%–80%
Oedema	Absent	Present
Mentation	Alert	Apathy, irritable
Mood	Normal	Irritable
Hair changes	Absent/mild	Present (flag sign)
Skin changes	Absent	Present (dermatosis, ulcers)
Muscle wasting	More (seen all over the body)	Less (seen only in the upper limbs as oedema masks wasting in the lower parts)
Organomegaly	Not present	Hepatomegaly (fatty liver)
Anaemia	Moderate	More severe
Subcutaneous fat	Grossly reduced	Less reduced
Investigations		
Serum proteins/albumin	Reduced	Markedly reduced
Serum enzymes	Normal	Decreased
Vitamin A absorption	Normal	Markedly reduced
Duodenal enzymes	Normal concentration	Reduced
Serum enzymes—amylase	Normal	Reduced

(Table continued)

TABLE 5.44 *(Continued)*

Features	Marasmus	Kwashiorkor
Urinary excretion (17-hydroxysteroids)	Increased	Low
Liver biopsy	No vacuolation	Fatty vacuolation
Complications	Less common and moderate	More common and severe
Response to treatment	Good	Variable
Mortality	More	Less

TABLE 5.45 Assessment of Nutritional Status

Classification	Parameters
Clinical assessment	Features of malnutrition Anthropometry Body mass index Growth chart
Morphological assessment by histological parameters	Hair morphology, buccal mucosal changes
Dietary assessment	24-hour recall method
Epidemiological assessment	Vital statistics—infant mortality rate, neonatal mortality rate, perinatal mortality, 1–4 year mortality, under-5 mortality rate
Biochemical parameters	Serum proteins (low albumin, α-1 and β-globulin) Urinary creatinine Serum amino acid pattern Serum lipids Blood sugar Minerals—potassium, sodium and copper Urinary hydroxy proline excretion index (HOP index)
Radiological parameters	Bone age

and signs of vitamin deficiencies are checked. The following anthropometric parameters should be measured:

- Weight
- Height
- Midarm circumference
- Head circumference
- Skinfold thickness
- Upper segment/lower segment ratio

Morphological Assessment

Morphological parameters are the changes that are seen externally in children with malnutrition. These comprise changes in the hair and mucosa. These are also known as histological parameters.

- Changes in hair morphology—the shaft of the hair is thinned. The mineral content of the hair root is decreased. Hair texture is altered at an earlier stage. Most of the cells in the growing end are in resting phase of telogen. Straightening of hair is present. In kwashiorkor, growing bulbs of hair decrease and the bulbs in resting phase increase.
- Buccal mucosal changes—the percentage of broken or mutilated cells in the buccal mucosa is 5%–10% in normal children. It may rise up to 70% in kwashiorkor.

Dietary Assessment

It is done by 24-hour recall method. Dietary assessment is based on the dietary intake of the present and past. Specific questions regarding breastfeeding, weaning, diet during and prior to illness, etc. are asked.

Epidemiological Assessment

The vital statistics reflect the nutritional status in a population. These include infant mortality rate, neonatal mortality rate, perinatal mortality rate, 1- to 4-year mortality rate and under-5 mortality rate. These rates are increased in kwashiorkor.

Biochemical Assessment

It is done by measuring nutrient concentration in the blood, urine, body fluids and tissues. Many biochemical changes are associated with malnutrition. The following tests are used to assess the nutritional status of the child.

1. Serum proteins—the visceral protein stores are assessed by measuring the serum proteins (albumin, prealbumin, retinol-binding protein). The total protein content depends on the globulin levels, but this is not used to assess the nutritional status. Albumin is decreased in

TABLE 5.46 Interpretation of Albumin Levels in Serum

Albumin Level (g/dL)	Significance
>3.5	Normal
3–3.4	Subnormal
2.5–2.9	Low
<2.5	Pathological

severe malnutrition (Table 5.46). Reversal of albumin/globulin ratio is seen in malnutrition. Serum transferrin <0.45 mg/dL is suggestive of severe malnutrition.

The frequency of assessment depends upon the half-life of the proteins. The half-life of albumin is 20 days, prealbumin 2 days and that of retinol-binding protein is 12 hours. The limitations of proteins in assessing the nutritional status of the child are:

- Positive and negative responses shown in acute phase reaction—albumin, prealbumin, retinol-binding protein and transferrin are negative acute phase reactants which decrease in response to infections. The positive acute phase reactants are C-reactive protein, ferritin, α-1-antitrypsin, etc.
- The production depends upon the synthetic function of an intact liver.

2. Serum amino acid pattern—ratio of non-essential to essential amino acids is measured as follows:

$$\frac{\text{Glycine + serine + glutamine + taurine}}{\text{Valine + leucine + isoleucine + methionine}}$$

Ratio	Inference
1.5	Normal
2–4	Subclinical PEM
>4	PEM

3. Lipid metabolism—serum β-lipoprotein, phospholipids and cholesterol are decreased in PEM. Serum lipoproteins are decreased in kwashiorkor but not in children with marasmus. Serum triglycerides are increased in marasmus and decreased in kwashiorkor.
4. Carbohydrate metabolism—blood glucose is decreased in severe malnutrition.
5. Minerals—low potassium (hypokalaemia), normal or increased sodium and decreased serum copper are seen in severe malnutrition.
6. Urine analysis:
   - Amount of creatinine excretion in the urine is constant between 1 and 5 years of age. Any decrease in the creatinine excretion in the urine should arise a suspicion of malnutrition.
   - Urinary hydroxyproline excretion index (HOP index)

$$\text{HOP index} = \frac{\text{Molecules of hydroxyproline/mL}}{\text{Molecules of creatinine/mL}}$$

Normal HOP index is 2–5. Less than 2 indicates retarded growth.

   - Urinary hydroxyproline excretion/creatinine ratio—this ratio usually rises in the first 3 months of life. After 3 months, the ratio starts falling. The rate of fall is more from 3 months to 4 years and then falls gradually. The ratio falls to adult level by puberty.
   - Urinary urea/creatinine ratio falls with decreased intake of proteins.
   - Urinary 3-methyl histidine excretion is decreased in PEM.
   - Urinary creatinine-height index (Table 5.47)

$$\frac{\text{24-hour urine creatinine}}{\text{24-hour creatinine for a normal child of same height}}$$

Radiological Assessment

Parameters like bone age should be assessed. Bone age is retarded and is less than chronological age in a child suffering from malnutrition. In chronic malnutrition, height is decreased. The bone age may correspond to height age. The following radiological findings may be seen:

- Osteoporosis

TABLE 5.47 Urinary Creatinine-Height Index and Its Significance

Urinary Creatinine-Height Index	Inference
1	Normal
0.25–0.75	Kwashiorkor
0.33–0.85	Marasmus

- Transverse lines at the long end of bones due to periods of arrested growth
- Features of scurvy
- Rickets—it is not manifested in severely malnourished child as the growth of bones is delayed. As rickets manifests in the growing bones, features of rickets will manifest during treatment

INVESTIGATIONS

Diagnosis of PEM is made by clinical assessment and anthropometry. However, following investigations may be done to support the diagnosis and to find out any associated infections and complications.

Investigations to Support the Diagnosis of PEM

- Serum proteins—total serum proteins, serum albumin and serum globulin. Total serum proteins and serum albumin are decreased, and there is reversal of albumin globulin ratio in kwashiorkor.
- Blood urea, serum creatinine, blood urea nitrogen (BUN)—usually decreased in marasmus due to decreased muscle mass. It is increased in marasmus with chronic renal failure which is associated with decreased intake due to loss of appetite and vomiting.

Investigations to Find Out Associated Conditions and Infections

1. Blood haemogram—Hb% decreased in anaemia
2. Peripheral smear study
   - Total WBC count—leucocytosis in pyogenic infections; may show leucopenia in severe sepsis
   - Differential leukocyte count—lymphocytosis in tuberculosis
   - Anaemia, leukopenia and thrombocytopenia in severe sepsis due to suppression of bone marrow
3. Erythrocyte sedimentation rate—increased in infections like tuberculosis
4. Blood culture—should be done to rule out sepsis
5. Liver function tests—bilirubin may be increased; SGOT and SGPT may be decreased in kwashiorkor
6. Stool examination
   (a) Macroscopic examination
      - Consistency—soupy consistency in lactose intolerance
      - Appearance—fatty stools in fat malabsorption

   (b) Microscopic examination
      - Ova, cyst (in hookworm infestation/giardiasis/amoebiasis/trichuriasis)
      - RBCs/pus cells in gastroenteritis, Crohn's disease

   (c) Biochemical examination
      - pH—acidic in lactose intolerance
      - Reducing substances—positive in lactose intolerance
      - Stool fat content—increased in fat malabsorption
      - Fat excretion—increased in children with fat malabsorption. It can be measured by fat absorption test, in which the child is given a diet containing less than 100 g of fat/day for five consecutive days. The fat excretion in the stool is measured for 5 days. Normal fat excretion is <5 g/day
      - Schilling test for absorption of vitamin B_{12}

Investigations to Find Out Specific Infections

Due to variable clinical presentation of infections in a malnourished child, the child should always be carefully evaluated for specific infections by the following investigations:

1. Peripheral blood smear for malarial parasite.
2. Chest X-ray—for associated respiratory infections.
   - Tuberculosis—miliary changes, hilar/paratracheal lymphadenopathy.
   - Bronchopneumonia—collapse/consolidation may be seen in immunodeficient

children following measles infection or marasmus.

3. Urine routine examination—should be done for presence of pus cells to rule out urinary tract infection. Chronic urinary tract infections are often associated with malnutrition.
4. Urine culture and sensitivity—chronic or recurrent urinary tract infections are associated with PEM.
5. Skin tests
   - Mantoux test—it is usually false-negative in PEM cases and in children below the age of 6 months. Delayed hypersensitivity is not developed which is responsible for the induration.
   - BCG test—accelerated BCG reaction may be seen in severely malnourished children.
6. Resting gastric juice examination for acid-fast bacilli—identification of acid-fast bacilli in sputum is diagnostic. Usually, children swallow the sputum and are not able to cough it out. Hence, examination of gastric contents from an empty stomach is done early in the morning in such children. This may show presence of acid-fast bacilli. The test is done for 3 consecutive days for better sensitivity.

Investigations to Detect Complications

1. Blood sugar—decreased in hypoglycaemia
2. Serum electrolytes
   - Potassium—hypokalaemia
   - Sodium—may be increased or decreased. Sodium levels are increased due to increased aldosterone. But in severe water retention, the sodium levels may be low due to dilutional hyponatraemia
3. Chest X-ray—heart failure, bronchopneumonia
4. ECG—heart failure

TREATMENT

The treatment of PEM consists of treatment of associated conditions and providing adequate calories and proteins for the proper growth of the child. The two basic steps in the treatment are dietary management and treatment of complications.

Grade I or Grade II PEM

In Grade I and Grade II PEM cases, usually the children are hungry, tolerate feeds orally and can be fed orally. These children can be managed at home by frequent feeding. Proper diet rich in calories and protein should be advised. At least 150 kcal/kg/day and 3 g/kg/day protein should be given. Adequate minerals and vitamins should also be provided. The best measure to assess response to therapy is weight gain.

Indications for Hospitalisation

The following are contraindications to domicilliary treatment:

- Anorexia
- Vomiting
- Diarrhoea
- Electrolyte imbalances
- Fever
- Severe infection

The child with the above features should be treated in a hospital.

Severe (Grade III or Grade IV) PEM

All cases of severe PEM should be managed in hospital. Treatment is given in two phases—stabilisation and rehabilitation. Phase of stabilisation consists of the resuscitative and the restorative phase. It aims at treatment of complications and attaining the normal weight for height. The rehabilitative phase aims at attainment of normal weight for age and continues for a longer duration (Table 5.48; see also Fig. 5.9).

Phase I: Stabilisation-Resuscitation Phase

The first step in the management of PEM is to save the life of the child. Hence, serious life-threatening complications associated with PEM should be addressed first. The following conditions are treated in the resuscitation phase:

TABLE 5.48 Treatment of Severe (Grade III or IV) PEM

Phase	Duration of Treatment	Management
Phase I (stabilisation)		
Resuscitative Phase	1–2 days	Hypoglycaemia Hypothermia Dehydration Electrolyte imbalances Anaemia, vitamin and micronutrient deficiencies Infections Congestive cardiac failure
Restorative Phase	3–7 days	Dietary management
Phase II		
Rehabilitative Phase	2–6 weeks	Nutritional counselling

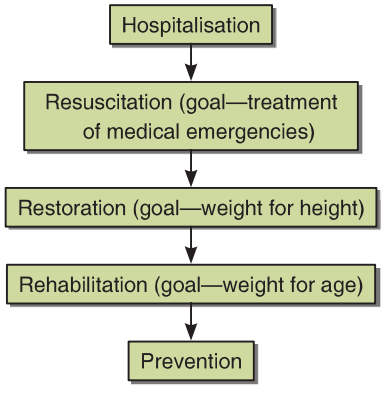
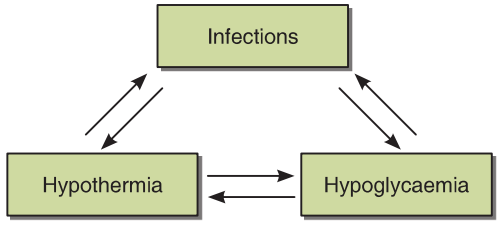


FIGURE 5.9 Steps in management of severe PEM.

- Hypoglycaemia
- Hypothermia
- Dehydration
- Electrolyte imbalances—hypokalaemia
- Anaemia, vitamin and micronutrient deficiencies—vitamin A deficiency, hypomagnesaemia
- Infections/infestations—associated systemic infections such as pneumonia, diarrhoea, urinary tract infections and worm infestations
- Congestive cardiac failure
- Convulsions, tremor and tetany

Hypoglycaemia, hypothermia and infections usually occur together in a malnourished child.



Hypoglycaemia. It occurs due to decreased intake, loss of reserves and increased catabolism (due to infection). It can be asymptomatic or symptomatic. Asymptomatic hypoglycaemia is diagnosed only by measuring the blood glucose levels. A high index of suspicion is necessary in malnourished children. Symptomatic hypoglycaemia presents with the following symptoms:

- Lethargy
- Unconsciousness
- Seizures

Other manifestations can be

- pallor and sweating,
- peripheral circulatory failure and
- hypothermia (axillary temperature less than 35°C or rectal temperature less than 35.5°C)

Treatment:

- Asymptomatic child—50 mL of 10% glucose solution is given orally or by nasogastric tube. Feeding is started 2 hourly day and night. To start with, the 2 hourly feed can be divided into four parts. Each part can be given every 30 minutes until the blood glucose level stabilises. Appropriate antibiotics should be started.
- Symptomatic child—hypoglycaemia should be treated with parenteral solution of 10% dextrose. 10% glucose 2–4 mL/kg is given IV as a bolus dose. Maintenance can be given as intravenous infusion of 10% dextrose. Feeding should be started as quickly as possible and continued 2 hourly day and night. Appropriate antibiotics should be administered.

Monitoring of blood glucose: If the blood glucose level is low, start treatment as recommended. Estimate the level again after 30 minutes by finger or heel prick method. Blood glucose monitoring should be done every 30 minutes until the blood glucose returns to

normal level and stabilises. Once the glucose level returns to normal, start 2 hourly feeding.

Prevention: Feed 2 hourly

- Feed regularly throughout the day and night
- Provide adequate warmth
- Treat infections with antibiotics

Hypothermia. The children with severe malnutrition are prone to develop hypothermia as they have low fat reserves and low metabolic rate. Low reading thermometer should be used for recording hypothermia in severely malnourished children. Rectal temperature <35.5°C (<95.5°F) or axillary temperature <35°C (<95°F) indicates the presence of hypothermia. The children with following conditions are prone to develop hypothermia:

- Marasmus
- Infections
- Denuded skin
- Infancy

Treat and prevent hypothermia. Warmth is provided by caring in warm environment, that is in a warm room under a radiant warmer. Child should be provided with warm clothes and kangaroo care to maintain normal body temperature (Table 5.49).

Severe hypothermia: It is said to be present in the children when rectal temperature falls below 32°C. Treatment of severe hypothermia is as follows:

- 5 mL/kg of 10% dextrose IV
- Intravenous antibiotics
- Warm humidified oxygen
- Heat
- Warm feeds
- Rehydration using warm fluids

TABLE 5.49 Methods to Provide Warmth

Mode of Transmission of Warmth to the Baby	Method of Providing Warmth
Conduction of heat	Warm, dry clothing Dry, warm surface Kangaroo mother care Handling with warm hands Warm feeds
Convection	Room heater
Radiation	Overhead warmer

Monitoring: Monitor temperature 2 hourly until the temperature returns to 36.5°C. Monitor temperature especially at night. Check for hypoglycaemia.

Prevention:

- Avoid frequent handling of the child
- Cover the child
- Avoid wet clothes
- Adequate feeds
- Rehydrate the child
- Minimise exposure of the child
- Prevent/treat infection with antibiotics
- Prevent/treat hypoglycaemia

Congestive Cardiac Failure. Congestive cardiac failure is common in children with kwashiorkor and can be missed. It should be treated with fluid restriction and diuretics. The fluid should be restricted to two-thirds of the requirement. Furosemide can be given in a dose of 1–2 mg/kg for diuresis. As the child is prone to develop hypokalaemia, potassium can be given along with furosemide; or potassium-sparing diuretic such as spironolactone can be given.

Digoxin should be avoided (Refer Chapter 8).

Dehydration. Treat and prevent dehydration. It may be missed in a malnourished child if not specifically looked for. This is because most of the clinical findings are common in both dehydration and malnutrition (Table 5.50). For instance, the skin turgor is lost and the child is irritable with weight loss in both malnutrition and dehydration. Oedema may be present in the presence of low blood volume. Dehydration in such children can be assessed by looking at the tongue for dryness. It is dry in dehydration and moist in malnutrition without dehydration. Tears may be absent in severe

TABLE 5.50 Differentiating Features between Marasmus and Severe Dehydration

Features	Marasmus	Severe Dehydration
Tongue	Moist	Dry
Tears	Present	Absent
Urine output	Normal	Decreased/absent
Pulse	Normal	Increased or decreased
Sensorium	Normal	Altered

dehydration.

Dehydration, if present, should be corrected as per guidelines. For treatment of dehydration, refer Chapter 7. A malnourished child should be given reduced osmolarity oral rehydrative salts (ORS) along with potassium supplements. Monitor hydration status every half hourly for 2 hours.

Prevention:

- Continue breastfeeding
- Initiate refeeding
- Give reduced osmolarity ORS between feeds for losses

Electrolyte Imbalances. Correct electrolyte imbalances with potassium supplements and restriction of sodium intake.

Hypokalaemia: It is common in severely malnourished children. It should be corrected slowly over a period of 24 hours in one of the following ways:

- Oral administration of potassium chloride solution—supplementation of potassium at 3–4 mmol/kg/day for at least 2 weeks.
- Administration of modified ORS with less sodium and extra potassium.
- Add 1 mL of potassium chloride to each 100 mL of intravenous fluid. The fluid infused should not contain potassium more than 40 mEq/L. Intravenous potassium is given only if the child is passing urine normally.
- In severe hypokalaemia (serum potassium less than 2 mmol/L or <3.5 mmol/L) with ECG changes—correct by starting potassium chloride in intravenous fluids at 0.3–0.5 mmol/kg/hour. If arrhythmias are present, provide 1 mmol/kg/hour of potassium chloride until the serum potassium normalises.

Precautions to be taken are as follows:

- Potassium should be avoided in presence of decreased urine output or renal failure.
- Hypokalaemia should be corrected slowly, as rapid correction can lead to hyperkalaemia (which predisposes to fatal cardiac arrhythmias).
- The child should always be monitored with an ECG while giving potassium infusion.

Hypernatraemia: It occurs due to increased ADH levels as a result of decreased inactivation by liver. This results in increased tubular reabsorption of sodium and water. Hypernatraemia should be corrected gradually by infusion of fluid containing 60 mEq/L of sodium. Salt-free fluids can be given orally. In presence of hypervolaemia, dialysis may be needed. In presence of dehydration, intravenous saline can be given.

Hyponatraemia: Total body sodium is increased but the plasma sodium is low in severely malnourished children. If there is water retention, it results in dilutional hyponatraemia. In cases with water excess like congestive heart failure, nephrotic syndrome and cirrhosis, sodium infusion expands the extracellular volume without correcting the hyponatraemia.

- If the sodium level is less than 120 mEq/L, 5 mL/kg of hypertonic saline (3% NaCl) can be given slowly over 3–4 hours.
- If the sodium level is more than 120 mEq/L, fluid restriction is helpful.
- Sodium to be given in mEq/L can be calculated by the following formula:

Sodium required (mEq/L)	=	(120 – actual sodium in mEq/L)	× 0.6 ×	body weight (kg)

This amount can be given as 3% NaCl which contains about 0.5 mEq of sodium per mL. Initial rapid correction should be aimed at raising the serum sodium level to 125 mEq/L only. Subsequent elevation should be in small increments of 5–10 mEq/L over 1–4 hours to raise the serum level to about 130 mEq/L. Rapid correction should not be done as it will precipitate central pontine myelinosis.

Infections/Sepsis. The classical features of infections like fever and leucocytosis may be absent in severely malnourished children. Broad-spectrum antibiotics should therefore be given to each diagnosed case of PEM even in the absence of clinical features of infection. These children often suffer from multiple infections; hence, they should be treated aggressively after sending blood for appropriate investigations.

- Pneumonia, diarrhoea, urinary tract infection—start with ampicillin 50 mg/kg/dose and gentamycin 7.5 mg/kg or amikacin 15 mg/kg to be given for 7 days. If the child shows no improvement within 48 hours, replace with cefotaxime 100–150

mg/kg/day 6–8 hourly or ceftriaxone 50–75 mg/kg/day 12 hourly.
- Meningitis—give cefotaxime 200 mg/kg/day 6 hourly and amikacin 15 mg/kg 8 hourly for 14–21 days.
- Malaria—antimalarials, if smear for malarial parasite is positive.
- Tuberculosis—antituberculous treatment should be started.
- Anaerobic infections—metronidazole 7.5 mg/kg 8 hourly for 7 days.

Worm Infestations. Deworming is done by albendazole 200 mg single dose in children below 2 years of age and 400 mg single dose in older children.

Dermatosis. Skin care should be given to prevent secondary infections. Impetigo should be treated with antibiotics. Frequent cleaning prevents colonisation of bacteria. Dry skin should be treated with emollients. Application of liquid paraffin is helpful as a barrier to infections as it is a poor culture media for organisms. Zinc deficiency may be associated with skin lesions and should be treated with zinc administration. Desquamation and ulceration should be checked and treated with application of 0.01% potassium permanganate solution. The perineal areas should be kept dry. Candida infection, if present, should be treated.

Shock. It should be treated with the following:
- Oxygen
- Intravenous glucose
- Intravenous antibiotics
- Intravenous fluids should be given slowly at 15–30 mL/kg of normal saline over 1 hour. The child should be assessed after 1 hour and if there is no improvement, blood transfusion 10 mL/kg is given slowly over 3 hours. Maintenance intravenous fluids 4 mL/kg/hour can also be given
- Inotropic agents—dopamine/dobutamine
- If the response is not good to the above treatment, intravenous steroids, epinephrine/norepinephrine can be given

Micronutrient Deficiency. Vitamins and mineral deficiencies should be treated. Vitamin supplementation can be done by infusion (1–2 mL daily), or as drops (0.3 mL and 0.6 mL daily in children younger than and older than 3 years, respectively) or syrup (2.5 mL/day for children over 3 years) orally.
- Vitamin A should be given in a dose of 1–2 lakh IU orally for first 2 days. For infants, 1 lakh units are given and for children aged more than 1 year, 2 lakh units can be given. The dose can be repeated after 2–4 weeks.
- Vitamin K can be given in a dose of 2–5 mg/day IM or IV for 2–3 days.
- Folic acid can be given in a dose of 1 mg/day.
- B-complex vitamins should be supplemented.
- Calcium deficiency (hypocalcaemia)—daily requirement is 10–20 mg/kg. Calcium deficiency is treated by slow infusion of calcium gluconate 1–2 mL/kg IV with equal amount of dextrose. This should be followed by oral administration of 50 mg/kg/day of elemental calcium in 2–3 divided doses. Heart rate should be monitored during treatment.
- Magnesium deficiency (hypomagnesaemia) results in seizures, tetany and apathy. $MgSO_4$ (50%) should be given intramuscularly in a single dose of 0.3 mL/kg (up to a maximum of 2 mL), or 0.1–0.2 mL/kg/dose can be given in 2 divided doses for 1–3 days. This should be followed by daily oral administration of 0.4–0.6 mmol/kg. Magnesium supplements can be added to the food.
- Iron should be given in a dose of 3–6 mg/kg/day for 3 months after the child starts gaining weight. It can be given for 6 months. Weekly iron given as a prophylactic measure is equally effective.
- Zinc deficiency—daily requirement is 1–2 mg/kg/day. Oral zinc compounds can be given in a dose of 50 mg/kg/24 hours in infants and 150 mg/kg/24 hours in older children. Zinc sulphate, acetate or gluconate can be given. Plasma zinc levels should be monitored.

Severe Anaemia
- Packed cell transfusion is given at 10 mL/kg. The infusion is to be given slowly over 3 hours.
- Blood transfusion may be given at 20 mL/kg.
- Diuretics should be avoided for oedema.

- The causes that predispose to anaemia should be treated.

Convulsions. Identify the cause and treat accordingly.

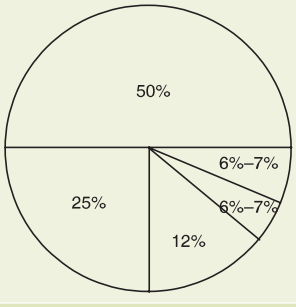
- 10% glucose IV
- 10% calcium gluconate—0.5–1 mL/kg
- 50% magnesium sulphate—0.2 mL/kg IM
- Vitamins B_1, B_6 and B_{12} and folic acid

Phase I: Restorative Phase

This is the second step in the management of severe PEM after stabilising the child. In children with mild-to-moderate malnutrition, this should be the first step in the management of PEM. This phase is to restore the weight for height. This includes dietary management.

Dietary Management. Before initiating the dietary management in a child with malnutrition, one should know about the basal metabolic rate and the normal distribution of calorie expenditure.

Normal calorie expenditure	
Basal metabolism	50%
Activity	25%
Growth	12%
Specific dynamic action (regulatory thermogenesis)	6%–7%
Stools—faecal loss	6%–7%



Basal metabolic rate

It is defined as the rate of energy expenditure at a state of complete rest. This constitutes about 50% or more of the total energy expenditure. It is measured under the following conditions:

- Complete physical rest
- At room temperature (20°C)
- Postabsorptive state—12–14 hours after last meal
- Half an hour mandatory rest
- Shortly after being woken up
- In the absence of any disease or fever
- Measured by indirect calorimetry

Basal metabolic rate in infants is about 55 kcal/kg/24 hours. This decreases to 25 kcal/kg/24 hours in older children.

Regulatory thermogenesis

It is the increase in metabolism over the basal rate by ingestion and assimilation of food, drugs, response to cold, etc. This is also known as specific dynamic action or the thermic effect of food. This is more for metabolism of proteins (29%) and less for carbohydrates (5%)

The total amount of food that is required by the child has to be built up gradually to fulfil the calorie and protein requirements.

- In the early stages, the child may not tolerate food orally. In such children, feeding should be started with nasogastric tube.
- Small oral feeds should be started as soon as possible.
- Breastfeeding should be continued.
- The diet should contain adequate calories, proteins, vitamins and minerals (Table 5.51). For malnourished children, RDA for the actual age should be used. In case the age is not known, the intake can be calculated for present weight.
- To start with, F-75 diet should be given which contains 75 kcal and 1.0 g protein in each 100 mL. Slowly F-100 diet should be introduced which contains 100 kcal with 2.5–3 g protein in each 100 mL.
- Cereal-based low lactose and low osmolarity F-75 diets should be given as starter diets in persistent diarrhoea. Osmolarity should be <350 mosm/L. Lactose content should not be more than 2–3 g/kg/day.
- There should be adequate bioavailability of micronutrients.

- Start with two-thirds of the calorie requirement and gradually step up the calorie content of the diet over 1 week to 10 days until the expected calories are supplied. Improve the calories content by making food isodense. Milk supplies about 70 kcal/100 mL. The calorie content can be increased to 100 cal/100 mL by adding sugar. Ghee and oil can be used to increase the calorie content without increasing the bulk of the food. This also does not increase the protein content of the food.
- The calorie intake should be increased to 150–200 kcal/kg/day and proteins to 4–6 g/kg/day (Table 5.51).
- Calorie gap or protein gap is the difference between the expected intake and present intake of calories or proteins, respectively. Total dietary recall is done. The calorie and protein gap is calculated. If the calorie gap is more than protein gap, more sugar and oil are added.
- Carbohydrates should supply 50%–55% of the total calories required. Fats should supply 30% of the total calories required and the proteins should supply 10%–15% of the calories required. Initially, proteins should supply only 5% of the total calories.
- The diet advised should be culturally acceptable, staple, digestible, affordable, easily prepared and easily available. It should be distributed evenly throughout the day. It should be a balanced diet containing animal protein or a cereal–pulse combination.
- 2 hourly feeds should be given for first 2 days followed by 3 hourly feeds for next 2 days. The duration between the feeds should be increased slowly (Table 5.52). Once the appetite returns to normal, the frequency should be brought down to six feeds/day and the volume of feeds should be increased.
- The quantity of foods should be increased in increments of 10 mL. The increments can be stopped once some of the food is left behind.
- Maximum volume per day should not be more than 130 mL/kg/day. In presence of oedema, the fluid can be restricted to 100 mL/kg/day.

Calculation of Diet for a 10-kg Child. A 10-kg child requires approximately 1000 calories and 25 g of protein. This can be given as per the sample diet chart shown in Table 5.53. Some items can be added or omitted according to the calorie and protein requirement of the child.

TABLE 5.51 Recommended Calorie and Protein Intake in Relation to Body Weight

	Present Weight of the Child	Expected Weight for the Age
Calories	150–200 kcal/kg/day	100 kcal/kg/day
Proteins	Vegetable protein is given 4–5 mg/kg/day Animal protein is given 3–3.5 mg/kg/day	1–1.5 g/kg/day

TABLE 5.52 Feeding Pattern as per WHO Guidelines

Days	Frequency	Volume of Feed (mL/kg/feed)	Vol/kg/day (mL)
1–2	2 hourly	11	130
3–5	3 hourly	16	130
6	4 hourly	22	130

TABLE 5.53 Model Diet for a 10-kg Child

Time	Food Item	Quantity	Calorie Value	Protein Content
7.00 am	Milk Sugar	150 mL 2 tsp	100 30	5 –
9.00 am	Idly Egg Oil	2 1 2 tsp	100 66 90	4 6 –
11.00 am	Ragi Sugar	6 tsp 2 tsp	100 30	2
1.00 pm	Rice Oil	1 cup 2 tsp	100 90	2 –
4.00 pm	Milk Sugar	150 mL 2 tsp	100 30	5 –
8.00 pm	Dosa Oil	1 2 tsp	50 90	2 –
Total			976	26

Modes of Feeding

1. Tube feeding—tube feeding may be needed in children who are unable to swallow. Nasogastric feeding is given by passing a nasogastric tube. The length of the nasogastric tube should be measured by measuring the distance from the tip

of the nose to the tragus and from tragus to the xiphisternum. The presence of the tube in the stomach can be confirmed by injecting air into the tube and auscultating for it over the stomach. The gastric emptying time may be increased in some patients. When most of the previous feed is remaining in the stomach, the next feed can cause distension of stomach and predispose to vomiting and aspiration. To avoid this problem, the stomach contents should be aspirated prior to each feed. If 50% of the previous feed is present in the stomach, one feed is skipped. If the entire previous feed is present, tube (enteral) feeds should be avoided. Parenteral nutrition (nutrition given by parenteral route) should be planned in such cases.

2. Parenteral nutrition—if the child is not tolerating oral feeds, a part of the required calories and proteins can be given parenterally.
   - Partial parenteral nutrition—if the child is not able to take feeds orally in adequate amount, part of the required calories and proteins can be infused. It is given only after the treatment of shock.
   - Total parenteral nutrition—it is the process by which the necessary calories, proteins, vitamins and minerals are supplied through a parenteral route. Total parenteral nutrition should be planned when all the previous oral feeds do not clear from the stomach. No oral feeds are given in such cases.

Phase II: Rehabilitative Phase

It consists of the following measures:

- Registration in nutrition clinic.
- Nutritional counselling—dietary advice, vitamin supplementation. Advise food containing high-energy and high-protein diet with micronutrients to rebuild wasted tissues. The RDA should be given to the child during this phase. Advise frequent feeding with easily available, cheap foods.
- Follow-up visits—should be organised every 3–4 weeks. During these visits, continuing care should be given. Weight monitoring, immunisation, vitamin supplementation and dietary advice should be taken care of even after discharge from the hospital.
- Vocational therapy—it is given to train the parents to do some work like stitching clothes, binding books and typewriting. so that they can earn some money. This can be used for purchasing food.
- Health education.
- Psychosocial stimulation should be provided to improve mental development.
- The diet should be advised keeping in mind the socioeconomic status and the cultural beliefs. Plant sources for proteins should be advised if patient is a vegetarian. The foods advised should be palatable, affordable and acceptable to the patient and the family.
- Nutritional supplementation—supplementary foods can be provided to the child by the health workers.

Signs of Recovery

The signs of recovery are as follows:

G	Catch-up growth
R	Return of normal motor activity Return of appetite Return of social smile; interaction with parents
O	Oedema disappears
W	Weight gain 70 g/kg/week Weight for height achieved by 8–12 weeks time

Response to treatment is indicated by rate of weight gain (Table 5.54).

Treatment Failure

Primary Failure

The treatment failure is said to be primary when the child does not improve after treatment.

TABLE 5.54 Weight Gain

Weight Gain	g/kg/day
Good	>10
Moderate	5–10
Poor	<5

Secondary Failure

Failure to gain weight of at least 5 g/day during rehabilitation phase is said to be secondary failure.

The clinical criteria for failure to respond to treatment are given in Table 5.55.

Complications during Treatment

The following conditions may be seen during treatment of a child with malnutrition.

Protein Overload Syndrome

It occurs within 2–3 weeks of treatment when the calorie intake is more than 250 cal/kg/day and protein intake is more than 6 g/kg/day.

Clinical Features. Cushing facies, oedema in legs, tachycardia, tachypnoea, cardiomegaly. All these features are due to a functional hyperthyroid and hyperadrenocortical state or probably due to high protein intake.

Treatment. Mainly symptomatic. The mainstay of treatment is to decrease the protein intake to less than 4 g/kg/day.

Encephalitis-like Syndrome

It is a self-limiting condition seen after 3–4 days of initiation of dietary therapy. Too much proteins in the diet result in this condition.

Clinical Features

- Coarse tremors
- Rarely progresses to unconsciousness
- Rigidity

TABLE 5.55 Criteria for Treatment Failure

Clinical Parameter	Day after Initiation of Treatment
Primary failure	
No appetite regain	Fourth day
Failure to start to lose oedema	Fourth day
Presence of oedema	Tenth day
Failure to gain weight at least 5 g/day	Tenth day
Secondary failure	
Failure to gain weight of 5 g/kg/day for 3 consecutive days	During rehabilitation phase

- Bradykinesia
- Myoclonus

Nutritional Recovery Syndrome

This is seen in children suffering from severe PEM who are under treatment with high quantity of proteins. It usually occurs by third week after starting treatment. This is a self-limiting condition and usually regresses by 6 weeks.

Pathogenesis

- Excess hormone secretion (like growth hormone, glucocorticoids) during recovery
- Dysmyelination
- Vitamin deficiency
- Neurotransmitter imbalance
- High solute load on the kidneys

Clinical Features

- Apparent deterioration with gynaecomastia and parotid swelling
- Abdominal distention
- Hepatomegaly
- Hypertrichosis
- Congestive cardiac failure
- Tremors—self-limited
- Spasticity

Investigations. Eosinophilia

Treatment. The child should be monitored along with contamination of nutritional therapy.

Pseudotumour Cerebri

The child may develop transient increased intracranial tension when the nutrition is corrected rapidly. This is a self-limiting condition.

Clinical Features

- Bulging anterior fontanel
- Vomiting

Prognosis

Prognosis depends upon early diagnosis and initiation of treatment. The development of nervous system occurs from 20 weeks of gestation to first 2 years of life. Hence, malnutrition at this age does not have long lasting effects on the CNS. Growth retardation and mental subnormality are long-term sequelae.

Poor Prognostic Factors

- Albumin level low—serum albumin <1.5 g%
- Bleeding—purpuric spots
- Consciousness—altered, coma
- Dehydration
- Dyselectrolytaemia—electrolyte imbalances like hyponatraemia/hypernatraemia
- Oedema (massive) with bipedal oedema
- Failure—circulatory failure and shock
- Grading of PEM—weight for height <70% of NCHS or <3 SD
- Hypoglycaemia
- Gastroenteritis
- Hypothermia
- Hepatomegaly—severe
- Infections
- Jaundice
- Kwashiorkor
- Lethargy
- Mental apathy—severe the degree, worse is the prognosis
- Muscle wasting—severe (MAC <11 cm)
- Micronutrient deficiencies—vitamin deficiencies

Late Prognostic Factors

Recovery may be late depending upon the following factors:

- Per capita income—higher the income, better is the prognosis.
- Literacy level of parents—higher the literacy, better is the prognosis.
- Environmental conditions—the prognosis is good when the environmental conditions are improved. In good environment, the chances of a child developing infections are low.
- Available healthcare facilities result in early diagnosis and treatment of child's illness.
- Size of the family—a child from a large family has chances of poor feeding and care.

Prevention

The following steps can be taken to prevent malnutrition:

1. Health education—as the child returns to the environment in which he/she developed nutritional deficiency, he/she may come back with malnutrition. To prevent malnutrition, the mother should be educated about the low-cost foods with good nutritive value. Also, the mother should be educated about preventing other conditions like diarrhoea which will precipitate malnutrition.
2. Three-plank protein bridge—a child is prone to develop PEM during the period of introduction of complementary feed. In the first 6 months of life, the risk of the child falling into the pit of PEM is very high. A practical plan known as three-plank protein bridge helps in preventing the child from falling into it (Fig. 5.10). To bridge this gap, three types of feed are advised which form the three planks of this protein bridge. These consist of animal protein, vegetable protein and prolonged breastfeeding.
3. In order to decrease the infant mortality, the following strategies have been formulated by UNICEF.
   (a) GOBIFFF
   - *G*rowth monitoring
   - *O*ral rehydration
   - *B*reastfeeding
   - *I*mmunisation
   - *F*eeding (supplementary)
   - *F*emale child care
   - *F*amily welfare

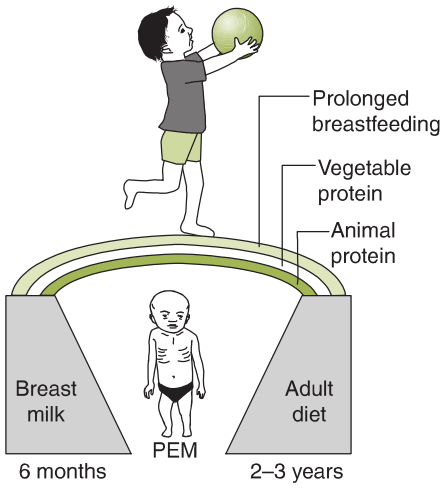


FIGURE 5.10 Prevention of PEM: three-plank protein bridge.

(b) SHAPOBI—as GOBIFFF did not cover the care for the mothers and the perinatal period, this was modified as SHAPOBI.

- *S*tatus for women
- *H*ealth education
- *A*ntenatal care
- *P*rimary healthcare and perinatal care
- *O*ral rehydration therapy
- *B*reastfeeding
- *I*mmunisation

(c) NIMFES

- Nutrition and growth monitoring
- Immunisation
- Medical check-up and medical care during illness
- Family planning
- Education—health education regarding care, child rearing skills and personal hygiene
- Stimulation

4. Preventing PEM at national level
   (a) Increasing the literacy rate, especially of the females
   (b) Increasing the crop production
   (c) Fortification of foods
   (d) Increasing the purchasing capacity of the people by creating employment opportunities
   (e) Nutritional education
   (f) Encouraging local food production
   (g) Improving health and nutritional status of adolescent girls
   (h) Providing good antenatal care for prevention of low-birth-weight babies

CHAPTER 6

Rickets

Rickets is a metabolic disorder characterised by defective mineralisation of growing bones despite normal collagen matrix. It results from various causes which include deficiency of vitamin D, its abnormal metabolism or the abnormal metabolism or excretion of inorganic phosphate and/or calcium. Osteomalacia is the defective mineralisation of the mature bone and is seen in adults. Osteoporosis is the reduction of bone mass per unit volume and it usually occurs in old age.

HISTORY TAKING

Name

It gives a clue of the religion or community to which the child belongs. Muslim females with *purdah* are more prone to develop rickets due to decreased exposure of the skin to sun rays.

Age

Age of onset of rickets will depend upon the cause of deficiency.

- Vitamin D-deficiency rickets is common in the age group of 6 months to 2 years, when the bones are growing rapidly.
- Familial disorders such as Fanconi's syndrome, cystinosis and 1-α-hydroxylase deficiency present at an early age.

Gender

- Rickets is more frequent in female children. This is because they are either not allowed to play outdoors, or they have to cover their whole body even when allowed to go outside in certain communities. Also, there is preferential nurturing of the male child and the female child may be neglected in certain families.
- If it occurs in males then it is usually more severe (vitamin D-resistant rickets, Lowe's syndrome).

Race

A fair infant whose area of the cheek of about 20 cm^2 is exposed to adequate amount of ultraviolet radiation can synthesise 10 μg of vitamin D which is enough to prevent rickets. Such an amount of exposure may not prevent rickets in a dark child.

Complaints

- Failure to thrive
- Bony deformities
- Generalised muscular hypotonia

History of Present Illness

- H/o delayed dentition
- H/o muscle weakness (generalised muscular hypotonia)

- H/o tetanic convulsions, carpopedal spasm, laryngeal spasm (in rickets associated with hypocalcaemia)
- H/o frequent incidences of fractures, recent onset bony deformities of spine (kyphosis, scoliosis), bowing of legs, knock-knees, rib-cage anomalies such as costochondral beading, pectus carinatum, and Harrison's sulcus

Aetiological History

1. Nutrition
   - Diet—adequate or inadequate
   - Dietary milk fortified with vitamin D or not
   - Animal products used in the food or not
2. Malabsorption—History suggestive of malabsorption syndromes
   - Failure to thrive
   - Symptoms suggestive of fat-soluble vitamin deficiencies (night blindness in vitamin A deficiency, petechiae and purpura in vitamin K deficiency, ataxia and tremors in vitamin E deficiency)
   - Abdominal pain
   - Distension
   - Steatorrhoea
3. Exposure to sunlight—adequate or inadequate
4. Renal rickets
   - H/o oliguria, polyuria, polydipsia, haematuria, dysuria, failure to gain weight, renal colic (occurs in RTA), vomiting, lethargy, growth retardation
   - H/o constipation, diarrhoea, vomiting (renal failure, renal tubular acidosis)
5. Hepatic rickets (chronic liver disease)—history of fever, jaundice, gastrointestinal bleeds (haematemesis/melena/haematochezia), neonatal hepatitis, itching (due to bile salts), purpura (due to liver failure)
6. Drugs
   - Anticonvulsants—phenytoin/phenobarbitone
   - Steroids
   - Outdated tetracyclines and heavy metals (predispose to Fanconi's syndrome)
7. Miscellaneous
   - H/o pain in abdomen—renal colic, lead poisoning, obstructive uropathy
   - H/o convulsion (glycogen storage disease, galactosaemia, Lowe's syndrome, cystinosis, renal osteodystrophy)
   - H/o fatigue, weight loss, bone pain (oncogenic rickets)
   - H/o alopecia (vitamin D-dependent rickets [VDDR] type II)

Past History

- H/o recurrent respiratory tract infections (cystic fibrosis, hypotonia of muscles in hypocalcaemic rickets)
- H/o jaundice (may be due to liver failure)
- H/o steatorrhoea (obstructive jaundice)
- H/o worm infestation (worms can enter the biliary tract and cause obstruction to the bile flow)
- H/o pica (common in worm infestations)
- H/o drug intake—anticonvulsants, steroid (antagonist to vitamin D), outdated tetracyclines (Fanconi's syndrome)
- H/o recovery from protein energy malnutrition

Antenatal History

- Maternal age at conception
- H/o maternal osteomalacia/maternal malnutrition (congenital rickets)
- Calcium supplementation during pregnancy
- Interval between two successive pregnancies (shorter interval will predispose to maternal malnutrition)
- Fever with rash (intrauterine infection), painful swelling behind the ears (postauricular lymphadenopathy in rubella)
- Drug intake (anticonvulsants), irradiation

Birth History

- Gestational age (full term/preterm)—prematurity is associated with osteopenia. Preterm babies are more prone to develop rickets as they require more vitamins for catch-up growth

- Mode of delivery (normal/caesarean)—when the mother has features of rickets, the pelvis may be triradiate type and normal delivery may be difficult
- H/o abnormal presentation (due to triradiate pelvis)

Neonatal History

- Low birth weight
- Breathing difficulties
- Birth asphyxia
- Neonatal convulsions
- Respiratory distress syndrome
- Kernicterus

Growth and Development History

- Short stature—the height or length is shorter than that expected for age
- The motor milestones may be delayed due to hypotonia of the muscles
- Mental retardation (Lowe's syndrome)

Personal History

- Personal likes and dislikes
- Indoor/outdoor activities
- Food fads
- Clothing pattern—wearing purdah

Family and Sibling History

- Consanguinity (VDDR, RTA distal type, 1-α-hydroxylase deficiency are familial)
- Inborn errors of metabolism
- H/o similar illness in the siblings (genetic, environment, nutritional causes of rickets)
- H/o chronic liver disease
- Maternal short stature (may be due to rickets)

Socioeconomic and Environmental History

- House—*pukka*/thatched
- Living area per family member
- Industrial air pollution (will decrease the amount of sunrays exposure)

CLINICAL EXAMINATION

General Examination

- Consciousness
- Undernourished/wasted (nutritional deficiency)
- Disproportionate short stature—the ratio between the upper segment and the lower segment will be abnormal (Table 6.1)
- Failure to thrive
- Hypotonia—ligaments are lax so that the joints can be bent to any position than in normal children

TABLE 6.1 Normal Ratio of Upper/Lower Segment at Different Age

Age	Upper/Lower Segment Ratio
At birth	1.7:1
6 months	1.6:1
1 year	1.5:1
2 years	1.4:1
3 years	1.3:1
4 years	1.2:1
7 years	1:1

Head-to-Toe Examination

The *skeletal manifestations* in the head-to-toe examination are as follows:

1. Head
   - Craniotabes—softening of skull bones (earliest). It occurs due to softening of the outer table of the skull bones and is better appreciated in the occipital region
   - Frontal and parietal bossing—giving box-like appearance of head known as hot cross bun appearance or caput quadratum. It occurs due to deposition of excess osteoid and non-calcified cartilage over frontal and parietal region
   - Prominent occipital protuberance (renal rickets)
   - Delayed closure of fontanels—anterior fontanelle remains wide open and its closure is delayed. Posterior fontanel which usually

closes within a few weeks after birth may also remain open
- Cranial sutures are widened
- Alopecia (VDDR type II)

2. Dentition
   - Delayed eruption of teeth
   - Premature fall of deciduous teeth
   - Defects in structure of teeth—enamel defects (hypoplasia) in permanent teeth, pulp defects (hypophosphataemic rickets), intraglobular dentine
   - Caries tooth (VDDR type I and hypophosphataemic rickets)
3. Chest
   - Harrison's sulcus (horizontal groove along the attachment of diaphragm, due to constant pulling of the soft lower ribs by the diaphragm)
   - Pectus carinatum or pigeon chest (forward projection of the sternum)
   - Pectus excavatum
   - Rachitic rosary—costochondral junctions are enlarged and beaded (smooth angle compared to sharp angle in scurvy) (Fig. 6.1)
   - Soft rib cage due to softening of ribs (predisposes to decreased chest movements and thereby atelectasis)
4. Spine
   - Kyphosis (rachitic cat back)—it occurs in children above 2 years of age due to softening of vertebra
   - Scoliosis
   - Lordosis
5. Extremities
   - Muscle weakness—the child is unable to stand till 3 years despite adequate weight and height due to proximal muscle weakness
   - Lower limb deformities become more pronounced once the child starts walking
   - Curvature or angulations at the junction of the lower and the middle thirds of the forearms and the legs. This is due to the softening of the bones
   - Anterolateral bowing of tibia at the junction of middle and lower one-third (Fig. 6.2)



FIGURE 6.1 Rachitic rosary (beading of ribs) in a child with rickets.

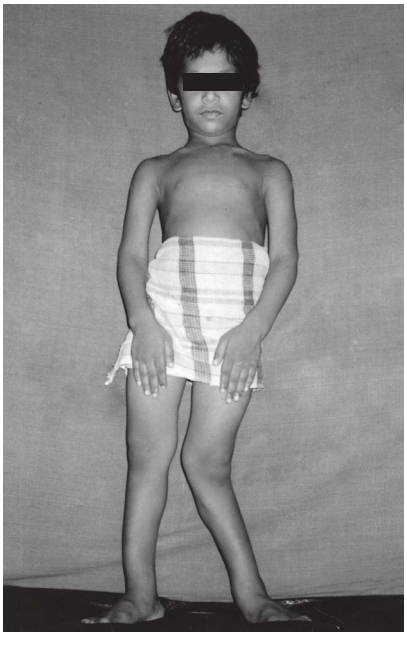


FIGURE 6.2 Widening of wrist, genu valgum left knee, varus deformity right tibia.

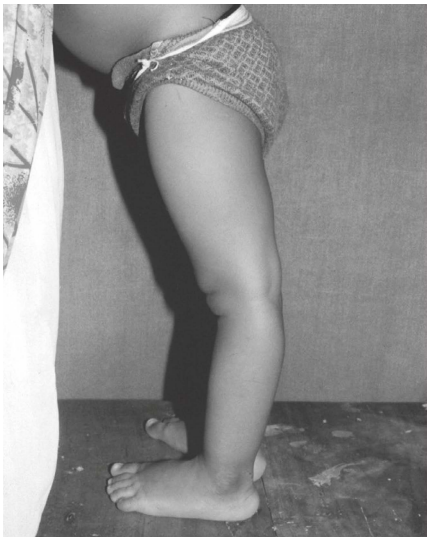


FIGURE 6.3 Genu recurvatum.

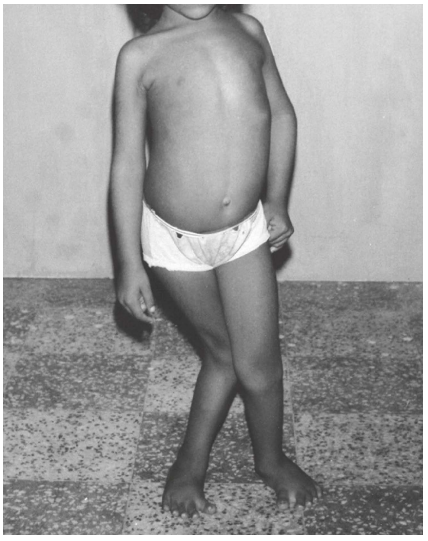


FIGURE 6.4 Right-sided coxa vara with right-sided genu valgum.

- Widening of epiphysis of wrists and ankles
- Double medial malleolus (marfan sign)—tibial malleolus gives an impression of double epiphysis
- Genu recurvatum—posterior angulation at the knee joints seen due to hyperextensibility of the knee joint) (Fig. 6.3).
- Genu varum (bowlegs)—the knees are bowed outside so the intercondylar distance is increased to more than 5 cm
- Genu valgum (knock-knees)—the knees are close to each other, but the intermalleolar distance is increased (>10 cm) (Fig. 6.4)

Genu valgum or varum can be differentiated clinically from tibial varum/valgum by the following method—on full flexion of knee, genu valgum/varum will disappear but tibial varum/valgum will remain the same. If the deformity does not disappear but reduces, then the valgum/varum is the result of both components; knee joint and tibial shaft.

6. Hip and Pelvis
   - Coxa vara deformity—reduction in femoral neck shaft angle (Fig. 6.5)
   - Triradiate pelvis—pelvic entrance is narrowed due to forward projection of promontory. Pelvic outlet will be narrowed due to forward displacement of the sacrum and coccyx



FIGURE 6.5 Bilateral coxa vara and genu valgum deformity in a child with rickets.

7. Joints and ligaments—the ligaments are lax and the limbs can be bent more than the usual (acrobatic rickets).

Systemic Examination

Extra-skeletal manifestations are seen during systemic examination.

Abdomen

- Pot belly (due to hypotonia)
- Liver and spleen are palpable due to downward displacement (visceroptosis—due to lax ligaments suspending the viscera)

Nervous System

- Irritability (due to hypocalcaemia)
- Laryngismus stridulus (sudden spasmodic laryngeal closure with crowing inspiration seen in tetany due to hypocalcaemia. This is often associated with cyanosis, apnoea, paraesthesia, tingling of hands and feet
- Seizures, tetany (due to hypocalcaemia)

Muscular System

- Hypotonia (due to hypocalcaemia)
- Proximal myopathy

Respiratory System

- Recurrent respiratory tract infections occur due to hypotonia

Findings Due to Complications and Associated Conditions

- Green stick fractures
- Slipped femoral epiphysis
- Fractures are common in rickets and renal osteodystrophy
- Wind-swept deformity (tackle deformity) where one knee goes for varus and other goes for valgus deformity
- Features of hypocalcaemia
- Features of malabsorption
- Features of hepatic/renal failure

INVESTIGATIONS

Confirmation of Diagnosis

Biochemistry

- Serum calcium—usually normal (10–12 mg/dL), may be decreased
- Serum phosphorus—inorganic phosphorus will be lower than the normal 4–6 mg/dL
- Calcium and phosphorus (PO_4) product should be 40 in normal children. In rickets, it will be less than 40
- Alkaline phosphatase—Increased due to increased osteoblastic activity

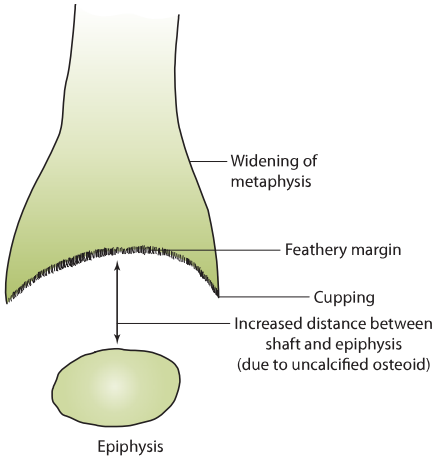
Radiological Changes

1. X-ray of skull shows widening of sutures
2. X-ray of ankle shows cupping and widening of the lower end of the tibia and fibula
3. X-ray of wrist (Fig. 6.6)

   (a) Changes in epiphysis
   - Delayed appearance of epiphysis
   - Widened epiphysis (flare)
   - Height of the physeal plate is increased due to lack of calcification of the newly formed bone (uncalcified osteoid)
   - Cupping of the margins at the end of the bones
   - Fraying at the margins at the end of the bone due to lateral bulging of osteoid tissue
   - Splaying

   (b) Changes in metaphysis
   - Widening of metaphysis
   - Cupping, exaggerated normal concavity and irregular calcification
   - Trumpeting (irregular end of long bones)

   (c) Changes in diaphysis
   - Thinned out cortex or pencil line cortex
   - Bending of long bones



(a)



(b)

FIGURE 6.6 (a) Radiological signs in rickets. (b) X-ray wrist showing widening, cupping and fraying of the distal ends of long bones in rickets.

- Rarefaction of the bones (density is decreased and the trabecula is prominent)
- Coarse trabecula
- Champagne glass appearance
- Double contour appearance of the shaft of radius (due to subperiosteal osteoid formation)
- Fractures, deformities (complications)—green stick fractures may be seen
- Healing rickets—a provisional zone of calcification between the shaft and the epiphysis
- The distance between the provisional zone of calcification and the epiphysis is more than the normal for the age
- Uncalcified osteoid causes an appearance that the diaphysis is separated from the periostium

Finding the Aetiology

- Complete blood count
- Liver function tests
- Renal function tests—blood urea and serum creatinine
- Serum electrolytes—potassium elevated in renal failure
- Urine proteins—aminoaciduria may be present
- Urinary pH
- Calcium and phosphate in urine and blood—phosphaturia (hypophosphataemia)
- Urine routine and microscopic examination

Other Investigations

- Tests for fat malabsorption
- Serum bicarbonate level decreased in acidosis
- 24-hour urinary calcium, phosphorus and bicarbonate levels

VITAMIN D

Before understanding rickets, one should understand the normal metabolism of vitamin D and physiology of bone formation. Vitamin D is available to the body in the following forms:

- 7-Dehydrocholesterol in skin is converted to cholecalciferol (vitamin D_3) on exposure to UV light
- Cholecalciferol (D_3) is also present in milk, milk products and animal fats
- Ergosterol is found in yeast. It can be converted to ergocalciferol (vitamin D_2)

Sources

- Egg, liver, milk, fish liver oils, butter and cheese
- Foods fortified with vitamin D
- Exposure to sunlight—whole body exposure for 30 minutes/week or head exposure for 2 hours/week to UV rays (296–310 nm) lead to synthesis of 10 μg of vitamin D

Daily Requirements

- Preschool children—400 IU/day (10 μg)
- Children—200 IU/day (5 μg)
- Pregnancy and lactation—400 IU/day (10 μg)

Metabolic Pathway of Vitamin D

1. *Skin:* 7-Dehydrocholesterol is present in the epidermal cells of the skin. It is converted to cholecalciferol (vitamin D_3) on exposure to sunlight. The rays which are useful in the vitamin D metabolism are ultraviolet radiation in sunlight (296–310 nm normal wave bands).
2. *Liver:* Cholecalciferol is hydroxylated in the liver to 25-hydroxycholecalciferol ($25(OH)D_3$) by hepatic microsomal enzyme (25-hydroxylase).
3. *Kidney:* $25(OH)D_3$ is hydroxylated in the kidneys by 1-α-hydroxylase to $1,25(OH)_2D_3$ (1,25-dihydroxycholecalciferol or calcitriol). This is the most active form of vitamin D. This is deficient in VDDR type I.

Metabolic pathway of vitamin D is summarised in Fig. 6.7.

Functions of Vitamin D

- Maintains normal serum calcium and enhances absorption of calcium and phosphorus from the gut.
- Stimulation of normal bone mineralisation and resorption—it mobilises calcium from bone when serum level decreases. It promotes mineralisation (calcium, phosphorus) of bone collagen, maturation and remodelling.
- Helps in the maintenance of growing skeleton and adult bones throughout the life (increased osteoblastic activity results in elevation of serum alkaline phosphatase).

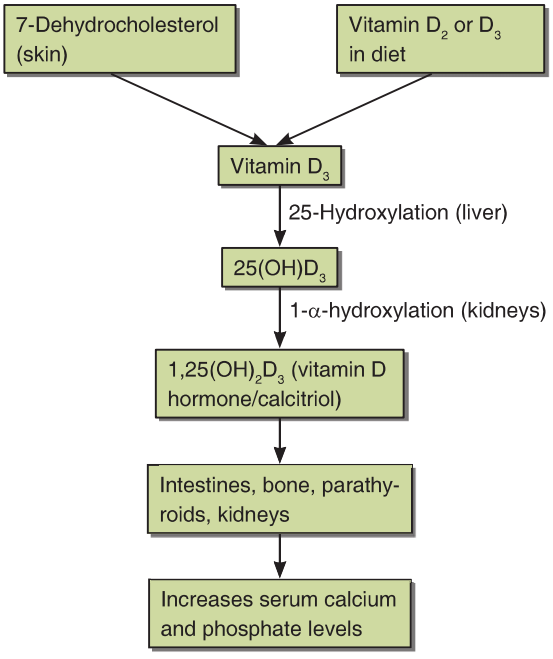


FIGURE 6.7 Metabolism of vitamin D.

- In kidney, vitamin D increases tubular absorption of phosphorus.
- Differentiation of keratinocytes and antiproliferative action against the cells in the skin.

Physiology of Bone Formation

There are three zones in the growing end of long bones (Fig. 6.8):

1. Resting zone of cartilage cells arranged in orderly fashion
2. Proliferative zone
3. Zone of mineralisation
   (a) Zone of preparatory calcification—the cartilage cells are swollen and degenerating in this zone. The matrix is impregnated with calcium salts
   (b) Degenerated cartilage cells are invaded by capillaries and osteoblasts. The osteoblasts deposit a layer of osteoid on the calcified cartilaginous trabeculae. This osteoid is converted into bone by deposition of calcium and phosphorus

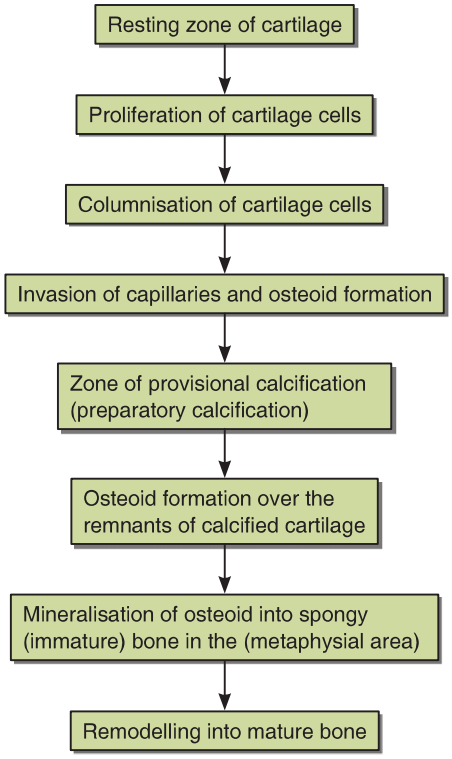


FIGURE 6.8 Steps in formation of bone.

CLINICAL FEATURES OF RICKETS

- Failure to thrive
- Disproportionate short stature
- Head—craniotabes, frontal and parietal bossing, delayed closure of fontanels, widening of cranial sutures, alopecia (VDDR type II)
- Dentition—delayed eruption of teeth, premature fall of deciduous teeth, defects in structure of teeth (enamel defects pulp defects, intraglobular dentine), caries tooth (VDDR type I and hypophosphataemic rickets)
- Chest—Harrison's sulcus, pectus carinatum, pectus excavatum, rachitic rosary
- Spine—kyphosis, scoliosis, lordosis
- Extremities—widening of epiphysis of wrists and ankles (double medial malleolus), genu recurvatum, genu varum, genu valgum
- Pelvis—coxa vara deformity, triradiate pelvis
- Abdomen—pot belly (due to hypotonia), visceroptosis (liver and spleen are palpable due to lax ligaments suspending the viscera)
- Nervous system—irritability, seizures, tetany due to hypocalcaemia
- Muscles—hypotonia (due to hypocalcaemia), proximal myopathy
- Respiratory system—recurrent respiratory tract infections due to hypotonia

CLASSIFICATION

Rickets is classified as follows:

I. *Vitamin D-deficiency rickets:* Responds to normal doses of vitamin D.
II. *Vitamin D-dependent rickets:* Responds to high doses of vitamin D.
III. *Vitamin D-resistant rickets:* Does not respond to even high doses of vitamin D.

VITAMIN D-DEFICIENCY RICKETS

It is also known as nutritional rickets or calcium-deficient rickets. The age of onset is usually between 6 months and 2 years. It may, however, present by 3–6 months of age.

Causes of Vitamin D Deficiency

Vitamin D deficiency can be primary or secondary.

1. Primary vitamin D deficiency—causes are as follows:
   (a) Decreased intake
      - Human milk/cow's milk contains low vitamin D
      - Lack of vitamin D in diet
   (b) Insufficient endogenous synthesis due to lack of exposure to sunlight (UV rays)—Whole body exposure to solar ultraviolet light will produce 250–625 μg (10,000–25,000 IU) vitamin D
2. Secondary vitamin D deficiency
   (a) Malabsorption—seen in the gastrointestinal tract disorders, pancreatic disorders and biliary tract disorders

TABLE 6.2 Secondary Deficiency of Vitamin D

System	Disorders	Mechanism
GIT and pancreatic disorders	Celiac disease Pancreatic insufficiency Cystic fibrosis	Impaired intestinal absorption of fat-soluble vitamin D
Liver disorders	Cirrhosis Biliary atresia Biliary tract obstruction Neonatal hepatitis Liver cell failure	Decreased absorption of fat-soluble vitamin D Decreased conversion of vitamin D_3 to $25(OH)D_3$
Anticonvulsants	Phenytoin Phenobarbitone	Induce hepatic cytochrome P-450 enzyme which converts $25(OH)D_3$ to polar vitamin D_3 (inactive form)
Kidney disorders	Chronic renal failure	Failure to convert $25(OH)D_3 \rightarrow 1,25(OH)D_3$

(b) Drug-induced rickets: Antiepileptic drugs such as phenytoin, phenobarbitone, carbamazepine, valproate and lamotrigine are associated with alterations in bone mineralisation in children. In such cases, vitamin D should be given prophylactically in doses of up to 2000 IU/day (Table 6.2)

Classification

Vitamin D-deficiency rickets is classified according to the age of the child at the time of exposure to its deficiency (Table 6.3).

I. Congenital rickets
- *Onset:* Neonatal period
- *Predisposing factor:* Maternal osteomalacia
- *Clinical features:* Skeletal deformities with tetany
- *Investigations:* Radiological features suggestive of metaphyseal lesion, widening, cupping, fraying of ribs and long bones can be seen in utero (or) at birth
- *Treatment:* IV calcium gluconate (or) oral calcium chloride with vitamin D 1000 IU/day should be given for 4–6 weeks. Calcium and phosphate supplement should be given

TABLE 6.3 Types of Vitamin D Deficiency Rickets according to the Age of Onset

Type of Rickets	Age of Onset
Congenital	Neonatal period with tetany
Premature	1–6 months
Infantile	6–12 months
Toddler	1–3 years
Adolescent	8–16 years

- *Prevention:* Detect and treat osteomalacia during pregnancy

II. Premature rickets
- *Age of onset:* 1–6 months
- *Causes:* Preterm/LBW, failure to give adequate vitamin D (800 IU) after birth
- *Clinical features:* Craniotabes
- *Investigations:* Radiological examination shows typical features of rickets
- *Treatment:* 2000 IU vitamin D daily orally for 4–6 weeks followed by maintenance dose of 400 IU daily. Calcium and phosphorus supplement should also be given
- *Prevention:* Prevention of prematurity, supplementation of vitamin D along with calcium and phosphate in premature babies

III. Infantile rickets
- *Age of onset:* 6–12 months
- *Predisposing factor:* Inadequate intake of vitamin D (<400 IU after birth) and use of cow's milk
- *Clinical features:* Bossing of skull, fiddle-shaped chest, rachitic rosary, thickened epiphysis. Clinical features do not appear in the weight bearing bones as the child is usually not walking by this age
- *Investigations:* Radiological examination shows typical features of rickets
- *Treatment:* 3000 IU vitamin D daily for 4–6 weeks followed by 400 IU daily
- *Prevention:* Continue fortified milk till 1 year of age along with supplementation of 400 IU vitamin D daily

IV. Toddler's rickets
- *Age of onset:* 1–3 years

- *Predisposing causes:* Daily intake of unfortified milk containing <100 IU of vitamin D
- *Clinical features:* Kyphosis, scoliosis; the child may be walking at usual age or have delayed walking
- *Investigations:* Radiological examination shows typical features of rickets
- *Treatment:* Vitamin D 3000 IU daily for 4–6 weeks followed by maintenance dose of 400 IU daily

V. Adolescent rickets

- *Age of onset:* 8–16 years
- *Predisposing factors:* Poor intake of vitamin D
- *Clinical features:* Bow legs, rachitic rosary
- *Investigations:* Radiological examination shows typical features of rickets
- *Treatment:* 3000 IU of vitamin D for 6 months followed by maintenance dose of 200 IU daily

Clinical Features

Clinical features of rickets have been discussed previously. Some of these according to the age of onset are as follows:

1. During first year
   - Cranium—craniotabes, wide sutures, frontal bossing
   - Wrist—widened
   - Ribs—rachitic rosary, Harrison's sulcus
   - Teeth—delay in eruption, enamel hypoplasia
   - Muscle weakness—unable to stand till 3 years despite adequate weight and height (motor milestone delay)
   - Recurrent respiratory infection—pneumonia
   - Tetany (or) stridor—in hypocalcaemia
2. After 1 year
   - Long bones deformities (due to rapid growth and weak epiphyseal plate—legs have most deformities)
   - Genu varum/valgum/recurvatum
   - Coxa vara
   - Rachitic saber shin
   - Up to 4 years of age they resolve with treatment
3. Late onset in childhood—long bones are straight, but knee epiphyses become angulated

Investigations

The investigation findings are as follows:

1. *Biochemistry:* Biochemical changes occur in three stages (Table 6.4). The findings are as follows:
   - Alkaline phosphatase level is increased. It is one of the earliest changes to occur in serum biochemistry. Normal levels are 5–15 Bodansky units or 15–20 king Armstrong units
   - Calcium levels may be normal/decreased
   - Phosphates level normal/decreased
   - Parathormone (PTH) levels increased
2. *Radiological changes:* These are predominantly seen in the wrists, knees, ankle and skull. The findings are as follows:
   - Widening of sutures of skull
   - Skeletal deformities—scoliosis, bowlegs, knock-knees, triradiate pelvis, etc.
   - Periosteal reaction
   - Cupping, fraying and splaying of metaphysis
   - Metaphyseal spur
   - Widening of epiphyses (flaring)
   - Thinned-out cortex
   - Coarse trabeculation
   - Zone of provisional calcification in healing rickets

TABLE 6.4 Sequence of Changes in Level of Serum Calcium and Phosphates in Rickets

Stage	Calcium	Phosphates
I	Decreased	Normal
II	Normal	Decreased (secondary hyperparathyroidism)
III	Decreased	Normal/decreased.

Treatment

1. Vitamin D
   - 1500–5000 IU/day orally for 6–10 weeks

- Single-day dose (Stross regime)—6,00,000 IU (intramuscular injection) or 15,000 μg of vitamin D_3 or cholecalciferol (orally in four to six divided doses)

Within 2–4 weeks, X-ray will demonstrate evidence of healing. Both the above given therapies should be followed by daily intake of 400 IU/day for 2–3 months until healing is well established and the alkaline phosphatase is approaching normal reference value. Alternatively, $1,25(OH)_2D_3$ (calcitriol) may be useful in cases with tetany but not for maintenance treatment

2. Other measures
   - Calcium supplementation (2–3 g/day in four divided doses)
   - Treatment of the cause
   - Exposure to sunlight
   - Treat associated vitamin deficiencies, anaemia, PEM
   - Treat associated infections and treat diarrhoea
3. Supportive therapy—if the baby is breastfed, supplement vitamin D and calcium to the mother
4. Diet
   - High calcium containing foods (calcium supplements)
   - Vitamin D containing foods such as fish, meat, cod-liver oil, egg yolk and butter
   - Dietary advice regarding addition of milk, egg, fish and meat in the daily diet

Follow-up and Response to Treatment

The healing starts between 10 and 15 days of administration of massive dose of vitamin D and is complete within 2–3 months. In nutritional rickets, phosphorus level rises in 96 hours and radiographic healing is seen in 6–7 days. In familial hypophosphataemic rickets, these changes will not be seen.

1. Biochemical changes
   (a) Early biochemical changes
   - Serum calcium decreased
   - Serum alkaline phosphatase increased (due to rapid skeletal mineralisation)
   - Urinary calcium increased (due to active skeletal mineralisation)

   (b) Late biochemical changes
   - Serum phosphorus levels will return to normal limits of 4–6 mg%
   - Serum alkaline phosphatase returns to normal (5–15 Bodansky units or 15–20 king Armstrong units) after several months
   - Resolving time of secondary hyperparathyroidism is not clear
2. Radiological changes
   (a) Thin radio-dense lines due to growth arrest in metaphysis, parallel to growth plate (Harris lines)
   (b) Calcification in the preparatory zone of calcification
   (c) Gradually, the whole zone of osteoid tissue is calcified and as healing progresses, there is an increase in the length of the bones
3. Clinical evidence of healing
   (a) Within 2 weeks, there is an improvement in muscle power and muscle tone
   (b) Normalcy returns in about 2–3 months
   (c) The bony changes and deformities, however, take time to regress

VITAMIN D-DEPENDENT RICKETS

It is also known as pseudovitamin D-deficiency rickets. It occurs despite adequate intake of vitamin D. The condition usually manifests in infancy and the clinical features are similar to that of deficiency rickets. The biochemical changes resemble those of nutritional rickets, but do not respond to physiological doses of vitamin D. Hence, it is called pseudodeficiency rickets. Large doses of vitamin D varying between 10,000 and 40,000 units daily are necessary for treatment which has to be continued life-long.

There are two types of VDDR

- VDDR type I
- VDDR type II

Vitamin D-Dependent Rickets Type I

It occurs as a result of 1-α-hydroxylase deficiency. It is inherited in an autosomal recessive manner.

Pathogenesis

1-α-Hydroxylation of cholecalciferol takes place in kidneys. Its deficiency results in low levels of formation of biologically active form $1,25(OH)_2D_3$.

Clinical Features

- Present with severe rickets
- Severe hypocalcaemia—laryngospasm, carpopedal spasm, seizures, myopathy
- Recurrent respiratory infections due to hypotonia

Investigations

- Calcium—low
- Phosphorus—normal
- Alkaline phosphatase—increased
- Parathormone—increased
- Low serum $1,25(OH)_2D_3$

Treatment

Prolonged high doses of vitamin D are required. Initial treatment is by massive dose of $1,25(OH)_2D_3$ (calcitriol) 0.5–2 μg/day. It is available as 0.25 μg tablet. Two to eight tablets can be taken daily. Lower doses can be used once rickets is healed. The aim is to maintain low normal serum calcium, normal serum phosphorus and high normal PTH levels. Periodic assessment of urinary calcium excretion should be done and it should be maintained below 4 mg/kg/day.

Prognosis

Manifestations recur on discontinuation of therapy.

Vitamin D-Dependent Rickets Type II

It is characterised by hereditary resistance to $1,25(OH)_2D_3$ (calcitriol). It is inherited as an autosomal recessive condition. Two types are seen—one associated with alopecia and the other not associated with alopecia.

Pathogenesis

- Point mutation affecting the structure or function of the receptors for calcitriol present in the skin, intestine and scalp
- There is a defect in the binding of 1,25-dihydroxycholecalciferol to its nuclear receptor along with defective nuclear translocation
- Inherited end-organ resistance to $1,25(OH)_2D_3$ despite its increased levels

Clinical Features

- Short stature
- Alopecia
- Abnormal teeth
- Tetany, spasm (hypocalcaemic features)
- Family history of alopecia and rickets may be present

Investigations

- Low calcium
- Normal phosphorus
- Elevated serum alkaline phosphatase
- Raised parathyroid hormone
- Increased serum $1,25(OH)_2D_3$
- No response to any form of vitamin D

Treatment

- These patients are resistant to treatment. They require high doses of vitamin D. Treatment is by massive dose of vitamin D_2 (2 lakh to millions IU)
- High doses of $1,25(OH)_2D_3$ (calcitriol) 15–60 μg/day with calcium supplements
- Long-term oral or intravenous calcium supplements in high doses

Prognosis

Healing rickets will be present. Alopecia does not get corrected.

VITAMIN D-RESISTANT RICKETS

In this variety, features of rickets develop despite regular daily administration of 400–1000 IU of

vitamin D. It is possible that in these children there is a mild defect in the conversion of vitamin D to its active metabolites.

Clinical Features

- Failure to thrive
- Marked deformities in infancy
- Marked delay in motor milestones
- Short stature
- Pallor
- Family history may be present
- High blood pressure
- Severe rickets without hypotonia

Classification

Vitamin D-resistant rickets is further divided into following groups:

I. Hereditary rickets
II. Rickets of renal origin
III. Oncogenic rickets—neoplastic rickets

Hereditary Rickets (Genetic Rickets)

It is mostly refractory to treatment with high doses of vitamin D. Genetic counselling should be done for inherited disorders. Hereditary disorders associated with rickets are as follows:

- Primary hypophosphataemic rickets
- Idiopathic hypophosphataemic rickets
- Autosomal recessive hypophosphataemic rickets with hypercalciuria
- Autosomal dominant hypophosphataemic rickets

Primary Hypophosphataemic Rickets

(Vitamin D-resistant rickets, X-linked familial hypophosphataemic rickets, vitamin D-non-deficiency rickets or refractory rickets). It is a rare disorder characterised by defect in proximal tubular reabsorption of phosphates and conversion of $25(OH)D_3$ to $1,25(OH)_2D_3$. It is the most common form of non-nutritional rickets.

Inheritance. It is X-linked dominant. Affected fathers have no affected sons but all their daughters are affected. Half of the daughters of the affected mothers will be abnormal.

Age and Gender. The onset occurs between the ages of 6 months and 5 years. The characteristic changes are present in the long bones. Males are more severely affected because they are homozygote with respective gene while the female carries a normal gene on the other X-chromosome. Females with hypophosphataemic rickets have less severe disease than males.

Pathogenesis. Genetic defect causes a kidney abnormality that allows high phosphate loss in the urine (phosphate wasting) inspite of low blood phosphates. The bones become painfully soft and bend easily.

- There is defective reabsorption of phosphates in the proximal convoluted tubules. Features of rickets develop due to deficiency of phosphate; blood contains low phosphate.
- There is also a defect in conversion of $25(OH)D_3$ to $1,25(OH)_2D_3$.

Clinical Features. The manifestations are more prominent in the lower extremities.

- Short stature
- Progressive limb deformities—resulting in waddling gait and bowing of lower extremities. Lower limbs are more involved than the upper limbs
- Coxa vara, genu varum, genu valgum
- Delayed dentition and pulp defects
- Features of hypocalcaemic rickets—tetany, rachitic rosary, Harrison's sulcus and profound myopathy will be absent

Diagnosis. It should be suspected in the presence of the following features:

- Clinical picture of rickets does not respond to usual doses of vitamin D (3000–5000 units daily for a period of 3–4 weeks or two massive doses of 6,00,000 units each, once in 2 weeks)
- There is osteomalacia despite normocalcaemia

Investigations

- Serum calcium—normal or slightly low
- Serum alkaline phosphatase—increased
- Serum phosphorus—low
- Parathormone—normal, no secondary hyperparathyroidism
- Calcitriol level—low or within normal range

- Urine—hyperphosphaturia (increased urinary excretion of phosphates despite low serum phosphorus)
- Radiological changes (metaphyseal widening, cupping, fraying) less severe than other types of rickets
- Oral phosphate tolerance test—defective absorption of phosphate in familial hypophosphataemic rickets
- There is no aminoaciduria, glycosuria, bicarbonaturia

Treatment

1. Medical treatment consists of the following:
   (a) Oral phosphates—0.5–1 g/24 hour (infants) and 1–4 g/24 hour (older children) in four to six divided doses. Joulie solution contains 30.4 mg of phosphorus per millilitre. It can be used in children. Commonest side effect of oral phosphate is diarrhoea.
   (b) Calcitriol ($1,25(OH)_2D_3$)—30–70 ng/kg/day in two divided doses. This is the preferred treatment. Alternatively, oral alfacalcidol can be given in a dose 25–50 ng/kg/day to children weighing less than 20 kg and 1 µg per day for those more than 20 kg. Excess calcitriol may lead to hypercalciuria and nephrocalcinosis. Hence, it is necessary to monitor treatment with investigations at regular intervals.
   (c) Adjuvant therapy—Amiloride and hydrochlorthiazide will reduce the risk of nephrocalcinosis.
2. Surgical treatment: It is done in very young children with deformity. It should be done along with the treatment of the metabolic cause. If the disease is not controlled metabolically, the deformity recurs even after corrective osteotomy.
   (a) Corrective splinting or bracing: For genu varum inner bar with outer strapping is given. For genu valgum outer bar and inner strapping are given to prevent progression of deformity and for correction (Table 6.5).
   (b) Corrective osteotomy: It is done after fusion of epiphysis. Both leg deformities can be corrected simultaneously. The goal of osteotomy is correction of deformity and alignment so that the plane of each knee joint is perfectly horizontal with the patient standing. For genu valgum, supracondylar osteotomy of femur is done. Genu varum is corrected by high tibial osteotomy (Table 6.5). Large doses of vitamin D should be avoided at least 3 weeks before surgery to avoid post-surgical hypercalcaemia (due to immobilisation). $1,25(OH)_2D_3$ has a short half life so it can be stopped just before surgery. Surgery should be undertaken after the serum alkaline phosphatase becomes normal.
   (c) Other procedures: Epiphysiodesis is done for bones before epiphyseal fusion. In this procedure, staples are placed across the growing epiphysis so that the opposite side grows normally to get the deformity corrected.

TABLE 6.5 Correction of Deformities in Rickets

Deformity	Corrective Splinting	Corrective Osteotomy
Genu valgum	Outer bar and inner strapping	Supracondylar osteotomy of femur
Genu varum	Inner bar with outer strapping	Osteotomy of tibia (high tibial osteotomy)

Prognosis. Adult height usually reaches 130–165 cm. With proper treatment an adult height of up to 170 cm can be achieved.

Idiopathic Hypophosphataemic Rickets

It is also characterised by defective renal tubular absorption of phosphates, but there are high levels of $1,25(OH)_2D_3$ and hyperabsorption of calcium. Investigations show hypercalciuria and a normal serum calcium level. This is different from X-linked familial hypophosphataemic rickets in which there is defective $1,25(OH)_2D_3$ production.

Autosomal Recessive Hypophosphataemic Rickets

It is characterised by increased urinary excretion of phosphates by the kidneys despite low phosphorus in

the blood (phosphate leak). The child may develop nephrocalcinosis which can be seen in the X-ray. Lab findings include increased levels of $1,25(OH)_2D_3$, normal calcium, phosphates decreased due to phosphate leak, increased alkaline phosphatase, hypercalciuria, parathyroid hormone normal or low. For treatment, phosphate supplements are given 0.5–3 g/day.

Autosomal-Dominant Hypophosphataemic Rickets

As the name suggests, it has an autosomal-dominant inheritance. There is an increased renal phosphate wasting with normal serum calcitriol. The renal phosphate wasting is not as prominent as in X-linked familial hypophosphataemic rickets.

Clinical Features. Short stature is not as prominent as in X-linked familial hypophosphataemic rickets

1. Group I
   - Bone pain
   - Weakness
   - No lower limb bone deformities
2. Group II
   - Lower limb bone deformities will be present
   - Improves after puberty

Treatment

- Oral phosphate
- $1,25\ (OH)_2D_3$ (calcitriol)

Rickets of Renal Origin

It refers to manifestations of rickets in association with certain renal pathology. It can be classified as follows:

- Glomerular rickets (renal rickets)
- Tubular rickets—seen in renal tubular acidosis, Fanconi's syndrome

Renal osteodystrophy is said to be present when the child presents with features of rickets in association with chronic renal failure.

Glomerular Rickets (Renal Rickets)

It is characterised by chronic glomerular insufficiency and is seen in conditions such as galactosaemia, Wilson's disease and Lowe's syndrome. The child presents with features of chronic renal failure. There is inability to convert $25(OH)D_3$ into $1,25(OH)_2D_3$. Impaired glomerular filtration will result in urea and phosphate retention, which results in lowering of blood calcium.

Clinical Features

- Bone pain—renal failure
- Mental retardation—Lowe's syndrome, galactosaemia
- Buphthalmos—Lowe's syndrome
- KF ring—Wilson's disease
- Cataract—galactosaemia, Wilson's disease, Lowe's syndrome
- Corneal deposits—cyst
- Alopecia totalis
- Hypothyroidism
- Cystinosis
- Hepatomegaly and jaundice—galactosaemia, Wilson disease
- Failure to thrive—chronic renal disease

Treatment

- Primary cause of renal failure should be treated.
- High doses of vitamin D should be given.

Tubular Rickets

It is characterised by defective tubular phosphate reabsorption resulting in phosphaturia and decreased phosphate levels. Retention of urea or creatinine does not occur.

- Proximal renal tubular acidosis (or type II RTA)—it usually occurs as a part of Fanconi's syndrome in which there is generalised proximal tubular dysfunction. This results in impaired absorption of phosphate, glucose, amino acids, bicarbonate and often proteins.
- Distal RTA (or type I RTA)—child usually presents with failure to thrive and bone demineralisation without overt rickets.

Oncogenic Rickets or Neoplastic Rickets

Soft tissue tumours and bone tumours secrete phosphatonin which will inhibit tubular reabsorption of phosphate resulting in phosphaturia and parathormone-like activity. Also, they impair the conversion of $25(OH)D_3$ to $1,25(OH)_2D_3$. The

following tumours are commonly associated with neoplastic or oncogenic rickets:

- Tumours of mesenchymal origin
- Neurofibromatosis
- Epidermal nevus syndrome
- Linear nevus syndrome

Investigations

1. Lab investigations
   - Phosphaturia and hypophosphataemia
   - Low serum calcium
   - Elevated alkaline phosphatase
   - Low or low-normal $1,25(OH)_2D_3$
   - Serum $25(OH)D_3$ levels—normal
   - Glycinaemia
   - Glycinuria
2. Radiological investigations
   - Scan for identifying the tumours
   - Bone X-ray for identifying the tumours

Treatment

Resection of the tumour—if the tumour cannot be resected the child can be treated with vitamin D_3 and phosphates.

Prognosis

Serum $1,25(OH)_2D_3$ levels raise to normal once the tumour is resected.

RENAL OSTEODYSTROPHY

Renal osteodystrophy is said to be present when features of rickets are seen in association with chronic renal disease or chronic renal failure. There is associated hyperphosphataemia.

Pathogenesis

- Early stage renal disease is associated with phosphate retention which suppresses vitamin D synthesis by kidney.
- Increased phosphate retention will cause increased binding of calcium in the gut. The patients will have secondary hyperparathyroidism.
- Late stage—acidosis causes demineralisation of bones because calcium gluconate acts as buffer.

Clinical Features

- Growth retardation
- Skeletal deformities
- Muscular weakness
- Bone pain

Investigations

- Blood urea, serum creatinine—elevated
- pH—acidosis
- Serum electrolytes—potassium elevated
- Calcium—decreased
- 1-α-hydroxylase—decreased
- X-ray—subperiosteal erosions, osteitis fibrosa cystica, nephrocalcinosis, rugger jersey vertebra (band-like regions of increased opacity at the superior and inferior margins of vertebral bodies)
- Ultrasonogram of abdomen—medullary nephrocalcinosis

Treatment

1. Diet low in phosphorus
2. Dialysis
3. Drugs
   - Phosphate binder—calcium acetate, calcium carbonate
   - High dose $1,25(OH)_2D_3$ (calcitriol/α-calcidiol)
   - Calcium carbonate

Differences between rickets and renal osteodystrophy are shown in Table 6.6.

COMPLICATIONS OF RICKETS

- Skeletal deformities
- Fractures are common in rickets and renal osteodystrophy
- Slipped femoral epiphysis

PREVENTION OF RICKETS

- Health education
- Exposure to early morning sunlight
- Fortification of foods with vitamin D
- Supplementation of calcium to pregnant and lactating mothers

TABLE 6.6 Differences between Rickets and Renal Osteodystrophy

Features	Rickets	Renal Osteodystrophy
Craniotabes	Present	Absent
Frontal bossing	Present	Absent
Involvement	Lower limbs and upper limbs are equally involved	Lower limbs are involved more than the upper limbs
Pathology	Failure of mineralisation of growing bone	Increased PTH activity (secondary hyperparathyroidism) Demineralisation due to excessive bone resorption
Radiological features	Widening, fraying and flaying of metaphysis	Less bone density Epiphyseal stippling Erosion of cortex Bone cyst Osteosclerosis
Response to therapy	Quick, early and adequate	Slow, delayed and often inadequate Lab evidence of renal damage (high phosphate levels) present

- Supplementation of the breastfed infants and low birth weight babies with calcium and phosphorus
- Vitamin D supplementation—daily oral administration of vitamin D in doses 350–400 IU (preterm), 800 IU (infants) and 1200 IU (adolescents)

DIFFERENTIAL DIAGNOSIS OF RICKETS

1. *Metaphyseal dysplasia:* Radiological features resemble those of rickets but this condition affects only few joints such as bilateral knee joints. Salient features are as follows:
   - Serum calcium and phosphorus—normal
   - Alkaline phosphatase normal
   - Usually symmetrical
2. *Hypophosphatasia:* The essential biochemical abnormality consists of low or absent alkaline phosphatase. Osteoblasts and hypertrophic chondroblasts are the principal source of phosphatase. There are various types according to age of onset—neonatal or perinatal form (lethal variety), infantile form (severe variety) and childhood form (associated with fractures, bone pain, milder skeletal abnormalities and premature tooth loss). It is inherited in an autosomal recessive manner (Table 6.7).
3. *Scurvy:* It occurs due to deficiency of vitamin C. Common clinical findings include irritability, bleeding gums, loose teeth, pseudoparalysis of limbs and scorbutic rosary.

Differentiating features between rickets and scurvy are given in Table 6.8.

TABLE 6.7 Differences between Rickets and Other Similar Conditions

Condition	Serum Calcium	Serum Phosphorus	Alkaline Phosphatase
Metaphyseal dysplasia	Normal	Normal	Normal
Hypophosphatasia	Normal	Normal	Low
Rickets	Low or normal	Low or normal	Increased

TABLE 6.8 Differences between Rickets and Scurvy

Features	Rickets	Scurvy
Aetiology	Vitamin D deficiency	Vitamin C deficiency
Symptoms	Painless	Painful
Rosary	Rachitic rosary—rounded	Scorbutic rosary—angulated
Pathology	Defective mineralisation of bone	Defective collagen formation
Radiological features	Thinned out cortex, cupping and fraying present White line of healing in healing phase of rickets Coarsening of trabeculae	Subperiosteal haemorrhages, fractures White line of Frankel Ground glass osteopenia
Primary symptom	Skeletal deformities	Gum bleeding
Bones	Easily bendable	Easily breakable

CHAPTER 7

Diarrhoeal Disorders

Diarrhoea is defined as the passage of three or more liquid or watery stools within 24 hours. Diarrhoea may have any of the following characteristics:

- Increase in frequency of stools
- Increase in fluidity of stools
- Increase in weight of stools

The change in consistency of stools is more important than the frequency. Hence, even a single episode of loose stool can be considered diarrhoea if the stools were previously formed. The normal stool output in children is 5 g/kg/24 hours. However, in diarrhoea the stool output is more than 10 g/kg/24 hours.

The following conditions are not considered diarrhoea:

- Frequent passage of formed stools (irritable bowel syndrome)
- Passage of pasty stools in a breastfed infant
- Passage of watery stools by a newborn after 3–4 days of birth
- Passage of stools during or immediately after feeding in a newborn (due to the initiation of gastrocolic reflex)

The watery stools passed by a newborn after 3–4 days of birth are called transitional stools. These stools are mucoid to watery, not foul smelling, and are not associated with dehydration. The frequency of stools may be up to 15 times per day. This condition is frequently mistaken for diarrhoea and the neonate is often referred to a paediatrician. No treatment is needed for this condition; reassuring the mother is sufficient if the baby is taking breastfeeds normally.

HISTORY TAKING

Age

Aetiology of diarrhoea differs as the child grows older. Causes of diarrhoea at different ages are given in Table 7.1. Infants below 3 months of age should be treated in a hospital as they are prone to complications.

TABLE 7.1 Causes of Diarrhoea According to Age of Onset

Age of Onset	Causes of Diarrhoea
6 months–2 years	Cow's milk protein intolerance Lactose intolerance
2–5 years	Celiac disease
>5 years	Inflammatory bowel disease
Older children	Irritable bowel syndrome Giardiasis Koch's abdomen
All ages	Gastroenteritis Antibiotic induced diarrhoea Food poisoning Sepsis

Sex

Toddler's diarrhoea is chronic non-specific diarrhoea due to maturational delay in intestinal motility. It is more common in boys.

Place of Residence

- Cholera should be suspected in a person who resides in an epidemic area.
- Food poisoning is common in places where there are poor storage facilities.
- Infections causing diarrhoea are common in areas affected by natural calamities such as flood.

Chief Complaints

An example of presenting complaints in a case of diarrhoea is as follows:

- Fever—3 days
- Loose stools—3 days
- Decreased urination—1 day

History of Present Illness

The history of present illness consists of details of the complaints in chronological order. The child should be enquired about the onset and progression of symptoms. Medical terminologies such as oliguria and melena can be used to describe the history of present illness.

The following should be enquired in the case of diarrhoea:

1. Onset—(acute/insidious)
2. Duration
3. Frequency
4. Stools (see Table 7.2)
   - Consistency watery/rice waterlike/semisolid
   - Colour
   - Volume (small or large)
   - Foul smelling or not
   - Character frothy/oily/sticky to pan
   - Associated with blood and/or mucous
   - Use of laxatives
   - Whether associated with drug intake
   - Presence of worms in stools
5. Precipitating and relieving factors—whether precipitated by particular type of food

TABLE 7.2 Characteristics of Stools in Specific Clinical Conditions

Disease	Characteristic Features of Stools
Lactose intolerance	Soundy, borborygmi Soupy consistency Sour taste (acidic pH) Sore bottom (due to acidic stools)
Fat malabsorption	Frequent Frothy Foul smelling Floats in water Fixes to the pan so that flushing will be difficult
Inflammatory bowel disease	Recurrent blood and mucous
Irritable bowel syndrome	Pellet- or ribbon-like stools
Starvation diarrhoea	Small, greenish, no faecal matter
Dysentery	Blood-stained stools
Cholera	Rice-water stools

6. Coexisting symptoms
   - Vomiting—time of onset of vomiting after food intake; number of episodes; type of vomitus (projectile/non-projectile); contents of the vomitus (Does it contain any undigested food particles?)
   - Abdominal pain/ball rolling movements in the abdomen—dysentery, IBD, pancreatitis
   - Fever
   - Tenesmus (feeling of difficulty during defecation)
   - Abdominal distension
   - Borborygmi (sound as the gas moves through the intestines)
   - Altered sensorium/convulsions
7. Features of dehydration—excessive thirst, drowsiness
8. Bladder history—urine output, burning during urination (urinary tract infection)
9. Oral intake—Does the child take feeds during the illness? Amount and the type of fluid taken by the child
10. Sometimes diarrhoea may coexist as a part of another illness. In such cases, it is important to assess the main complaint for which the patient has come to the hospital. Some examples are given in Table 7.3

TABLE 7.3 Main Symptoms of Clinical Conditions in which Diarrhoea Is also Present

Presenting Complaint	Disease/Condition
Wheeze	Food allergy, cystic fibrosis
Arthralgia	Inflammatory bowel disease
Flushing	Carcinoid syndrome
Jaundice	Bile acid diarrhoea
Recurrent respiratory infections	Immunodeficiency
Ataxia	Abetalipoproteinaemia

11. H/o drug intake which may predispose to side effects that may resemble diarrhoea or its complications. Hence, before assessing a child with diarrhoea, one should ask for intake of drugs given as follows

Drug	Side effects
Ampicillin	Loose stools
Furazolidone	Vomiting
Antiemetics	Drowsiness
Antispasmodics	Retention of urine

History of Past Illness

History of similar illness in past should be enquired.

Treatment History

1. H/o hospitalisation
   - Duration of stay in hospital
   - Nature of treatment
   - Any complications
2. H/o drugs—antibiotics-induced diarrhoea
   - Antineoplastc drugs (can cause enteritis)
   - Antibiotics—ampicillin (can cause diarrhoea)
3. Radiation—radiation enteritis
4. H/o native treatment

Contact History

History of contact with a known case of tuberculosis should be confirmed.

Antenatal History

- Booked or unbooked case
- Antenatal infection with *Listeria monocytogenes* is associated with diarrhoea in a newborn

Birth History

- Full term/preterm (preterms are prone to infections and breast milk intolerance)
- Mode of delivery (babies delivered vaginally are prone to aspirate *L. monocytogenes* or *Escherichia coli* from the mother, both of which can predispose to diarrhoea in a newborn)

Neonatal History

Low birth weight (are prone to infections)

- Prematurity
- Birth asphyxia
- Septicaemia (can present with diarrhoea)
- Intra-abdominal sepsis (can present with diarrhoea)
- Procedures—umbilical cord catheterisation will predispose to septicaemia
- Umbilical sepsis will predispose to septicaemia

Growth and Development

- Any delay in the milestones (motor and mental)
- Retardation in physical growth (chronic diarrhoea due to malabsorption, disorders or protracted diarrhoea)

Family and Sibling History

The history of the following illnesses in other family members is checked.

- Acute diarrhoea (amoebiasis, giardiasis or food poisoning)—in case of food poisoning, the examiner should enquire about the food taken, the time interval between the food intake and the onset of diarrhoea. Incubation period for staphylococcal food poisoning is 2–3 hours
- Chronic diarrhoea (malabsorption syndrome, celiac disease, inflammatory bowel disease, cystic fibrosis, food allergy)
- Jaundice (chronic or acute liver disease)
- Chronic cough (tuberculosis, cystic fibrosis or alpha-1 antitrypsin deficiency)

Socio-Economic History

- House—*pukka*/thatched
- Living area per family member
- Per capita income
- Water and sanitation facilities
- Any other relevant details (like environment)—factories such as pencil manufacturing factories (lead) and motor vehicle workshops (lead) letting out toxic substances and contaminating water.

Nutritional History

1. Enquiries about diet during onset of illness, during episodes of diarrhoea and during remissions.
2. Enquiries about food allergy or intolerance to certain foods by asking the following:
   - Diarrhoea following the intake of cow's milk—cow milk protein allergy
   - Diarrhoea following the intake of wheat—celiac disease
   - Diarrhoea following the intake of milk—lactose intolerance
   - Diarrhoea following the intake of diet containing sugars—can be seen in sucrase/isomaltase deficiency
3. Effect of withholding food—in osmotic diarrhoea if the food is withheld, the frequency of loose stools decreases.

GENERAL EXAMINATION

1. Consciousness—normal/altered sensorium/unconscious
2. General appearance—the child looks chronically ill
   (a) Nutritional status of the child undernourished/well nourished
   (b) Signs of nutritional deficiency
      - Acrodermatitis enteropathica—zinc deficiency
      - Dermatitis (pellagra—niacin deficiency)
      - Signs of vitamin D deficiency (in malabsorption syndrome)—bossing, open anterior fontanel, alopecia
      - Vitamin A deficiency (in malabsorption syndrome)—Bitot's spots, corneal/conjunctival xerosis or ulcer
3. Signs of dehydration—sunken AF, sunken eyes, absence of tears, dry tongue
4. Pallor
5. Jaundice
6. Clubbing—celiac disease, cystic fibrosis, IBD
7. Lymphadenopathy—for tuberculosis, leukaemia and lymphoma
8. Erythema nodosum—IBD
9. Pedal oedema (due to hypoproteinaemia in protein energy malnutrition or protein losing enteropathy)
10. Oral cavity—oral thrush (common in immunodeficiencies)
11. Skin
    (a) Purpura, ecchymosis (DIVC in septicaemia, thrombocytopenia in haemolytic uremic syndrome following *Shigella* infection)
    (b) Scratch marks—bile acids in hepatic conditions (steatorrhoea)
12. Hands
    - White nails (due to hypoalbuminaemia in protein losing enteropathies)

Vital Signs

- Pulse—weak in severe dehydration
- Temperature—hypothermia in severe dehydration
- Respiratory rate—tachypnoea (due to acidosis)

EXAMINATION OF ABDOMEN

Inspection

1. Abdominal distension—uniform or localised
2. Flanks—free or full
3. All quadrants move well with respiration
4. Veins of abdominal wall—visible, dilated, tortuous
   - Position—anterior/lateral/back
   - Direction of flow in the veins
5. Visible gastric pulsations
6. Visible intestinal pulsations
7. Skin—stretched, shiny

- Scars—sinuses
- Look for plasters, after certain procedures like tapping

8. Hernial orifices
9. External genitalia

Palpation

- Soft/tense
- Local tenderness
- Guarding/rigidity
- Palpable masses

Auscultation

Normal frequency of bowel sound is 3–5 sounds per minute. It should be checked whether they are decreased or increased.

RECTAL EXAMINATION

In cases with dysentery, rectal examination is essential to rule out other causes of rectal bleeding.

EXAMINATION OF OTHER SYSTEMS

The examiner should look for the presence of associated infections such as pneumonia, otits media and urinary tract infections.

Cardiovascular System

In cases with dehydration, there will be tachycardia, in early stages, followed by bradycardia.

Respiratory System

In severe dehydration, respiratory rate is increased if metabolic acidosis is present (acidotic breathing).

Central Nervous System

- Altered sensorium
- Irritability in moderate dehydration
- Drowsiness in severe dehydration

CLASSIFICATION OF DIARRHOEA

According to Duration

Depending on the duration, diarrhoea can be classified as follows:

1. *Acute diarrhoea* usually lasts for less than 7 days but can persist up to 14 days.
2. *Chronic diarrhoea* lasts for more than 14 days and is of non-infective origin.
3. *Persistent diarrhoea* starts as acute diarrhoea but lasts for more than 14 days. It is associated with a series of enteral infections without any time to recover between the episodes of diarrhoea. There may be persistent colonisation of small intestines with microbes. Most cases are due to *Giardia lamblia* causing simple disaccharide intolerance and respond to diet modifications.
4. *Protracted diarrhoea* lasts for more than 14 days and is associated with malnutrition. Both persistent and chronic diarrhoeas are associated with this condition (Table 7.4). It does not respond to diet modifications such as avoiding sugar.

TABLE 7.4 Classification of Diarrhoea according to Duration

Classification of Diarrhoea	Duration of Diarrhoea	Aetiology
Acute diarrhoea (<14 days) • Acute self-limiting diarrhoea • Acute, prolonged or indeterminate diarrhoea	 3–7 days 8–14 days	Infective
Chronic diarrhoea	Loose stools for >2 weeks	Non-infective; causes are inflammatory bowel disease, immunodeficiency and malabsorption
Simple persistent diarrhoea	≥14 days	Begins as infective origin
Persistent protracted diarrhoea	≥14 days with malnutrition	

TABLE 7.5 Aetiological Agents Causing Diarrhoea

Type of Organisms	Organisms
Small-bowel diarrhoea	
Viruses	Rotavirus, Norwalk virus, astrovirus, calcivirus, coronavirus
Bacteria	*Vibrio cholerae*, enterotoxigenic *E. coli*
Parasites	*Giardia lamblia, Strongyloides stercoralis, Cryptosporidium parvum*
Large-bowel diarrhoea	
Bacteria	*Shigella*, enteroinvasive *E. coli*, enterohaemorrhagic *E. coli, Salmonella, Campylobacter jejuni*
Parasites	*Entamoeba histolytica, Trichuris trichiura, Balantidium coli*, schistosomiasis

According to Site of Pathology

1. Small-bowel diarrhoea
2. Large-bowel diarrhoea

The aetiological agents causing small- and large-bowel diarrhoea are given in Table 7.5, and their differentiating features are given in Table 7.6.

According to Mechanism of Diarrhoea

Osmotic Diarrhoea

It occurs due to non-absorption of substances such as carbohydrates (as in lactose intolerance), due to the ingestion of substances that cannot be digested or absorbed or due to any condition that results in decreased digestion or absorption.

As the food is not absorbed, the osmotic pressure increases. This results in decreased absorption of water and electrolytes. The amount of fluid that enters the lumen exceeds the resorptive capacity of the colon. This fluid is lost in the stools, which is seen in the following conditions:

1. Malabsorption—lactase deficiency, glucose–galactose malabsorption
2. Ingestion of unabsorbable solutes—intake of lactose, lactulose, magnesium, polyethylene glycol, sorbitol
3. Intake of fruit juice containing large amounts of sucrose and fructose
4. Short gut syndrome

TABLE 7.6 Differences between Small-Bowel and Large-Bowel Diarrhoea

Features	Small-Bowel Diarrhoea	Large-Bowel Diarrhoea
Volume of stools	Large	Small
Colour	Light	Dark
Frequency	Not very frequent	Frequent
Odour of stools	Offensive	Odourless
Nature of stools	Bulky, watery, steatorrhoea or frothy explosive stools	Loose stools with blood and mucus or jellylike
Bloating of abdomen	Present	Absent
Effect of defecation on abdominal discomfort	Relieved	Not relieved
Borbogymi and flatulence	Present	Absent
Tenesmus	Absent	Present
Constitutional symptoms	Not common	Fever and prostration
Vomiting	More common	Rare
Dehydration	Present	Usually absent
Perianal excoriation	Present	Rare
Causative agents	*Vibrio cholerae*, *E. coli*, rotavirus, Norwalk virus, giardiasis	*Shigella*, *Entamoeba histolytica*
Complications	Dehydration	Haemolytic uremic syndrome Toxemia

5. Infections such as *G. lamblia*

The malabsorbed carbohydrates are metabolised in the colon by colonic bacteria to substances that further contribute to the increased osmotic pressure and aggravate osmotic diarrhoea. The features of osmotic diarrhoea are as follows:

1. This type of diarrhoea stops on stopping the offending agents or on starvation. This occurs again on refeeding with the offending agents.
2. The pH of the stools is decreased in carbohydrate malabsorption (pH <5 can be seen).
3. Perianal excoriation is seen in carbohydrate malabsorption.
4. Stool for reducing substances is positive in sugar intolerance.

5. Prone to develop hypernatraemia.
6. The faecal osmolar gap (FOG) is calculated as: serum osmolarity − (2 × [faecal sodium + potassium concentration]). FOG is increased in osmotic diarrhoea (FOG >100 mOsmol/L)
7. Stools are large, frothy and explosive.

Secretory Diarrhoea

There is an active secretion of fluid into the gut. It occurs either due to infection with organisms such as cholera and *E. coli* or due to certain drugs and other conditions as given below:

1. Exogenous factors
   (a) Infections—enterotoxigenic bacteria (toxins of *Vibrio cholerae*/*E. coli*). These are the most common cause of secretory diarrhoea. The toxins lead to the failure of sodium pump which is responsible for the absorption of fluid in the gut
   (b) Laxative abuse—anthraquinone cathartics, castor oil
   (c) Drugs—quinine, colchicines, prostaglandins
   (d) Unabsorbed dietary fat
2. Endogenous factors
   (a) Bile acid malabsorption—terminal ileal disease
   (b) Defective transport of sodium or chloride (congenital chloridorrhoea)
   (c) Endocrine tumours—produce secretagogues. Here are some examples:
      - VIPoma (vasoactive intestinal peptide)
      - Zollinger–Ellison syndrome (gastrin)
      - Carcinoid tumours (histamine, serotonin, polypeptide)
      - Neuroblastoma, medullary carcinoma of thyroid (calcitonin and prostaglandins)

The features of secretory diarrhoea are as follows:

- Diarrhoea persists despite starvation
- Stool osmolality is 290 mOsmol/kg (normal osmolality)
- pH >6
- Osmotic gap <100 mOsmol/L
- Stool sodium >70 mEq/L

Differences between osmotic and secretory diarrhoea are given in Table 7.7.

Exudative or Inflammatory Diarrhoea

There is damage to the epithelial cells and mucosa of the gut as a result of bacterial and parasitic

TABLE 7.7 Differences between Osmotic Diarrhoea and Secretory Diarrhoea

Features	Osmotic Diarrhoea	Secretory Diarrhoea
Effect of fasting on stool frequency and consistency	Decreased symptoms	No change
Appearance	Not ill looking	Ill looking
Stools	Large volume, semisolid	Large volume, watery
Flatulence	++	–
Perianal excoriation	Present	Absent
Withdraw the offending agent	Diarrhoea stops	Does not respond
Dehydration	+	++
Volume of stools	<200 mL/24 hour	>200 mL/24 hour
Stools consistency	Soupy—lactose intolerance	Watery
Volume of stools	Proportional to amount of intake of offending foods	More
Investigations		
Stool osmolality	400 mOsmol/kg ↑osmolality > 2 × ($Na^+ + K^+$)	290 mOsmol/kg Normal osmolality = 2 × ($Na^+ + K^+$)
Stool sodium	Less	More
Stool Na^+	<70 mEq/L (30 mmol/L)	>70 mEq/L (105 mmol /L)
Stool K^+	30 mmol/L	40 mmol/L
Stool pH	<5	>6
Evidence of malabsorption	Present	Absent
Stool for reducing substances	Positive	Negative
Solute gap	280 mmol/L	0 mmol/L
Osmotic gap	>100 mOsmol/L	<100 mOsmol/L

infections. The stool contains blood, pus, mucous and proteins. Common causative organisms are *Salmonella, Shigella, Yersinia, Campylobacter* and *Clostridium difficile.*

Diarrhoea Due to Altered Motility

Diarrhoea can also occur due to increased or decreased intestinal motility as in irritable bowel syndrome and pseudo-obstruction. This is due to decreased absorption time during rapid transit and due to bacterial overgrowth during slow transit.

Pathological Classification

On the basis of pathogenesis and severity, infectious agents (such as bacteria and virus) can produce two types of diarrhoea, specified as below:

Non-Inflammatory Diarrhoea

It occurs due to enterotoxins produced by some bacteria (*Staphylococcus aureus*, *Bacillus cereus* have preformed toxins), adherence by parasites/bacteria and destruction of villus by viruses.

Inflammatory Diarrhoea

It occurs due to direct invasion by bacteria and cytotoxin production.

The differences between non-inflammatory and inflammatory diarrhoea are given in Table 7.8.

TABLE 7.8 Differences between Inflammatory Diarrhoea and Non-inflammatory Diarrhoea

Features	Inflammatory Diarrhoea	Non-inflammatory Diarrhoea
Pathogenesis	Direct invasion of the intestine by bacteria -Cytotoxin production by bacteria	Enterotoxins production by bacteria, destruction of villi by viruses, parasites adhere to the mucosa
Causative agents	*Shigella* *E. coli* (invasive) *C. difficile* *Aeromonas* *Campylobacter* *Salmonella* *Y. enterocolitica* *E. histolytica*	*Vibrio cholerae* *Aeromonas* *E. coli* (enterotoxigenic) Rotavirus Norwalk virus Calicivirus Astrovirus

Inflammatory diarrhoea is suspected when a child presents with acute bloody diarrhoea. If the stools contain blood and mucous, it is also known as *dysentery.* Such stools are accompanied by abdominal cramps and fever. Dysentery can be caused by bacteria or amoeba. Their differentiating features are given in Table 7.9. Dysentery is commonly due to *Shigella* in children under 5 years. It should be treated with antibiotics.

Other Types

Factitious diarrhoea: Self-inflicted diarrhoea due to excessive use of beverages, carbohydrate intake, junk foods, laxative abuse.

Indeterminate diarrhoea: It is difficult to find out the cause at presentation.

TABLE 7.9 Differences between Bacterial and Amoebic Colitis

Features	Bacterial Colitis	Amoebic Colitis
Causative agents	*Shigella* Enteroinvasive *E. coli*	*E. histolytica*
Age	Any age	Common after 2 years of age
Constitutional symptoms	Common	Rare, can be seen in fulminant and extraintestinal amoebiasis
Abdominal pain	Crampy, lower abdominal pain relieved by defecation	Less significant
Tenesmus	Significant	Less significant
Duration of illness	Short	Prolonged
Rectal examination	Oedematous rectal mucosa Blood and mucus with no faecal matter	Ulcerated mucosa Rose pink coloured stool staining
Treatment	Appropriate antibiotics	Metronidazole
Complications	Haemolytic uremic syndrome Toxemia	Fulminant and extraintestinal amoebiasis

Spurious diarrhoea: It is due to overflow in rectal stasis (Hirschsprung's disease).

Starvation diarrhoea: In patients with starvation, stools are small, greenish, frothy and contain little faecal matter. There is an associated weight loss.

Bile acid diarrhoea: In ileal resection, bile acid is not absorbed and enterohepatic circulation is disrupted.

Functional diarrhoea: Non-organic recurrent abdominal pain with loose stools, diagnosis is by exclusion of other causes, no nocturnal diarrhoea; long duration of diarrhoea but no associated weight loss.

Fatty diarrhoea: Fatty stools due to fat malabsorption, occurs in pancreatic or severe small-bowel disease.

Traveller's diarrhoea: It occurs in persons travelling to developing countries.

Toddler's diarrhoea: Chronic non-specific diarrhoea, common between 6 months and 3 years of age, also known as 'chronic diarrhoea of infancy' in young children.

Parenteral diarrhoea: Diarrhoea due to infections outside the GIT. Common causes are UTI and otitis media (Table 7.10).

Pseudodiarrhoea: Hyperdefecation occurs in hyperthyroidism due to increased sympathetic activity.

Hypermotility diarrhoea: Irritable bowel syndrome.

Surgical causes of diarrhoea: Acute appendicitis, intussusception, Hirschprung's disease, short bowel syndrome

TABLE 7.10 Parenteral Diarrhoea

Causes	Conditions
Infections	Systemic infections—septicaemia, respiratory tract infections
Metabolic disorders	Diabetic ketoacidosis
Endocrine	Adrenal insufficiency, hyperthyroidism, congenital adrenal hyperplasia
Genitourinary	Urinary tract infections
Nutritional	Acrodermatitis enteropathica
Others	Reye's syndrome, neuroblastoma, ganglioneuroma

ACUTE DIARRHOEA

It refers to diarrhoea lasting for less than 14 days.

PREDISPOSING FACTORS

- Infants
- Malnutrition
- Infections—measles
- Low socio-economic class
- Immunodeficiency disorders
- Antimalignant therapy
- Irradiation
- Bad child rearing practices
- Drugs such as ampicillin

CAUSES

1. Enteral infections
   - Viruses—rotavirus, enterovirus, Norwalk virus, adenovirus, calicivirus, coronavirus, astrovirus
   - Bacteria—*V. cholerae*; enterotoxigenic, enteroinvasive, enteropathogenic and enteroadherent *E. coli*; *Salmonella; Shigella*; *Campylobacter*; *S. aureus*; *C. difficile*; *B. cereus*; Enterobacteria; *Klebsiella*; *Yersinia enterocolitica*; *Pseudomonas aerunginosa*; *Campylobacter jejuni*; *Aeromonas hydrophilia*
   - Parasites—*Entamoeba histolytica* (amoebiasis), *G. lamblia*, *Cryptosporidium*, *Strongyloides stercoralis*
   - Fungi—*Candida albicans*
2. Parenteral infections
   - Urinary tract infections
   - Septicaemia
3. Drugs—antibiotic-associated diarrhoea (*C. difficile* toxin)
4. Rotavirus and enterotoxigenic *E. coli* are the commonest causes of diarrhoea in children

INVESTIGATIONS

1. Examination of the stool
   - Macroscopic—colour, consistency, presence of mucous and blood

- Microscopic—pus cells/leucocyte more than 10 cells/HPF, RBCs, evidence for the infecting agents (parasites/bacteria, protozoa, fungus), helminths, ova, cyst
- Hanging drop examination for cholera
- Stool for reducing substances
- Stool pH

2. Stool culture (when cholera, *Shigella*, *Salmonella*, *Pseudomonas*, *Campylobacter* are suspected)
3. Tests for malabsorption
4. Sigmoidoscopy/colonoscopy
5. S. electrolytes
6. Blood gas estimation
7. Renal function test

MANAGEMENT

The management of a patient with acute diarrhoea depends on the assessment and analysis of the clinical situation.

Assessment	Dehydration Nutritional status Sepsis screening Feeding habits Weight Associated symptoms such as fever
Analysis	Note the type of diarrhoea (acute/chronic) Whether associated with passing of blood in stools Whether associated with malnutrition
Action	Treatment of dehydration (Plan A, Plan B, Plan C)

Assessment of Dehydration

The following points should be assessed:

- Fluid deficit—severity of dehydration (Table 7.11; also see Fig. 7.1)
- Type of dehydration (Table 7.12)
- Electrolyte disturbance (hyponatraemia, hypokalaemia)
- Acid–base disturbances
- Assessment of the renal function

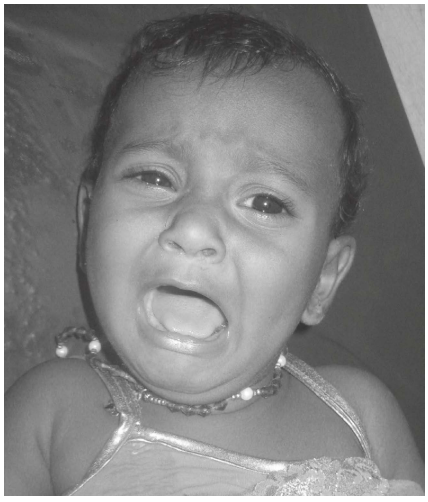


FIGURE 7.1 Irritable child with some dehydration.

Treatment of Dehydration

The dehydration is treated with fluids given either orally or intravenously. Fluid therapy is based on three components:

1. Correction of existing water and electrolyte deficit
2. Replacement of ongoing losses
3. Provision of normal daily fluid requirements

Oral Rehydration Therapy

Principle of oral rehydration—glucose-dependent sodium co-transport is unaffected in acute diarrhoeal diseases.

Oral rehydration therapy (ORT) includes the following:

1. Oral rehydration solution (ORS)—WHO recommended ORS (also recommended by Indian Academy of Paediatrics), low osmolarity ORS, cereal-based ORS, fortified ORS, etc. (Tables 7.13 and 7.14)
2. Other fluids and liquid diets—sugar and salt solution (SSS), home-available fluids

ORS

I. *WHO ORS:* There are two types of WHO ORS available in market—conventional ORS and low osmolarity ORS.

TABLE 7.11 Assessment of Severity of Dehydration

Features	No Dehydration	Some Dehydration	Severe Dehydration
Sensorium[a]	Alert	Irritable	Lethargic/unconscious
Thirst[b]	Not thirsty; drinks normally	Thirsty; drinks eagerly	Drinks poorly or not able to drink
Skin turgor[c]	Normal	Goes back slowly	Goes back very slowly
Eyes[d]	Normal; tears present	Sunken; tears absent	Very sunken; tears absent
Oral mucosa[e]	Moist	Dry	Very dry
Definition	No signs of dehydration	If two or more of the above signs, including at least one key sign, are present, then the patient is in some dehydration.	If two or more of the above signs, including at least one key sign, are present, then the patient is in severe dehydration.
Weight loss	<3%	3%–9%	>9%
Heart rate	Normal	Normal; may be increased	Tachycardia; bradycardia in most severe cases
Pulse	Normal	Normal to decreased volume	Weak, thready or impalpable
Extremities	Warm	Cold	Cold, mottled and cyanotic
Treatment plan	Plan A	Plan B	Plan C

[a–e]Signs used to assess the severity of diarrhoea. Of these, [1–3] are key signs.

[c]Skin turgor has less importance in infants and malnourished children.

[e]Mouth can be dry in a mouth breather or can be wet if the child has recently vomited or has consumed something orally.

TABLE 7.12 Features of Specific Types of Dehydration

Features	Isotonic	Hyponatraemic	Hypernatraemic
Incidence	70%–80%	10%–15%	<5%
Pathogenesis	Loss of isotonic fluid	Loss of sodium-rich fluids	Increased sodium administration or fluid loss exceeds sodium loss
Causes	Diarrhoea with vomiting, simple enteritis	Cholera, sweating, viral diarrhoea	Diabetes insipidus, administration of faulty prepared ORS
Serum osmolality	281–297 mEq/L	<281 mEq/L	>297 mEq/L
Serum sodium	133–145 mEq/L	<133 mEq/L	>145 mEq/L
Symptoms	Apathy, lethargy	Altered sensorium	Irritability
Skin turgor	↓	↓↓	Normal
Skin feel	Dry	Clammy	Thick, doughy
Mucous membrane	Dry	Dry	Parched
Pulse	↑	↑↑↑	↓
Treatment	½ Isotonic solution for 24 hours followed by isotonic solution	0.9% NaCl solution	Hypotonic solution 0.2% NaCl with 5% dextrose for 24 hours followed by ½ Isotonic solution
Comments	Most common type	Can result in cerebral oedema, so it should be corrected rapidly	Should be corrected very slowly, over 48 hours or more. The decline in sodium should be about 0.5 mEq/L or 12–15 mEq/day
Complications	Metabolic acidosis Pre-renal failure	Cerebral oedema	Intracranial haemorrhage due to shrinkage of brain cells

TABLE 7.13 WHO ORS (Conventional versus Low Osmolarity)

Ingredients	Ingredients per Litre (g)		Components	Concentration of Ingredients per Litre (mmol/L)	
	High Osmolarity ORS	Low Osmolarity ORS		High Osmolarity ORS	Low Osmolarity ORS
Sodium chloride	3.5	2.6	Sodium	90	75
			Chloride	80	65
Trisodium citrate dehydrate	2.9	2.9	Citrate	10	10
Potassium chloride	1.5	1.5	Potassium	20	20
Glucose	20	13.5	Glucose	111	75
Total osmolarity				311	245

TABLE 7.14 Composition of Different Low Osmolarity ORS

Ingredients	mEq/L (mmol/L)	mEq/L (mmol/L)	mEq/L (mmol/L)
Sodium	50	60–70	75
Chloride	40	60–70	65
Potassium	20	20	20
Citrate	30	10	10
Glucose anhydrous	111	75–90	75
Osmolarity	251	210–260	245

Disadvantages of conventional WHO ORS (high osmolarity):

1. Poor acceptability due to taste.
2. Increases volume, purge rate and duration of diarrhoea.
3. It has a high sodium concentration of 90 mmol/L. This provides too much sodium, which is dangerous to oedematous children. Congestive cardiac failure can occur in these patients when associated with anaemia.
4. Because of the potential risk of hypernatraemia, it may not be an optimal solution to correct the dehydration status in severely malnourished children.

Advantages of low osmolarity ORS over conventional ORS:

1. Treatment of acute diarrhoeal disease in newborn and young infants.
2. The reduced osmolarity ORS is as effective as standard ORS in adults with cholera.
3. Reduced osmolarity ORS promotes more effective water and sodium absorption than the WHO ORS.
4. There is less stool output and decreased frequency of vomiting and no additional risk for developing hypernatraemia.
5. More stability of reconstituted solution.
6. Decreases number of hospitalisations.
7. Advantage of the reduced osmolarity ORS formulation for general use including malnutrition is that a single formulation would be promoted for all ages, irrespective of aetiology or nutrition status.

II. *Cereal-Based ORS/Rice-Based ORS (Super ORS):* The rice-based ORS is clearly superior to WHO ORS in efficacy in patients with cholera; the two solutions had similar efficacy in non-cholera diarrhoea.

Advantages:

1. Decreased purge rate
2. Slow release of glucose from starch

III. *ORS with Micronutrients:* Micronutrients help in absorption of water and sodium.

1. *Zinc-fortified ORS*: Advantages are:
   - Modifies the course of diarrhoeal illness
   - Decreases severity of diarrhoea
   - Prevents recurrent episodes of diarrhoea
2. *ORS fortified with amino acids*: Oral rehydration solutions fortified with amino acids such as L-alanine glycine, glutamine—all have high osmolarity. This has been more efficacious in cholera but is not as effective in non-cholera diarrhoea in children.

IV. *Other types of ORS*

1. ORS in severely malnourished children with dehydration (ReSoMal). This is a rehydration solution for the severely malnourished children who have potassium deficiency but have high

levels of sodium. They also have a deficiency of magnesium, zinc and copper. So the use of the standard WHO ORS is dangerous in them. Potassium concentration of standard WHO ORS cannot replace the potassium. Hence, an ORS solution with potassium 40 mEq/L and sodium 45 mEq/L with magnesium, zinc and copper has been recommended by WHO for use in the severely malnourished children.

2. *Home-made ORS (sugar–salt solution)*: 4 g salt and 40 g sugar added to 1 L of water.

Precautions to be taken while giving ORS:

1. High-fibre diet should be avoided along with ORS.
2. ORS should be given in small sips or, preferably, with a spoon.
3. If there is vomiting, ORS should be given after 10 minutes.
4. If vomiting is severe, intravenous fluids should be given.
5. Staple food should be given. Rice with milk or curd and sugar can be given.

Home-available fluids

Recommended	Not recommended
• Lemon water • Rice water • Soups • Dal water • Lassi • Coconut water • Plain water	• Simple sugar solution • Glucose solution • Carbonated soft drinks • Fruit juices—tinned or fresh • Fluids for athletes • Gelatin desserts • Tea/coffee

Many of these fluids lack a glucose precursor, salt or both, or these are not present in specified amounts. Therefore, these are likely to be effective only in presence of continued feeding which provides starch (ultimately glucose) and protein (ultimately aminoacids) to promote absorption of luminal sodium. These fluids together with food provide ORT.

The advantages of using the home-available fluids are easy availability, low cost, easy to prepare, acceptable taste and culturally acceptable.

ORT will be ineffective in the following cases:

- High purge rate
- Persistent vomiting
- Paralytic ileus
- Shock
- Glucose malabsorption
- Incorrect preparation
- Improper administration of ORS

Plan A—Treatment of Diarrhoea in Children with no Dehydration

It is followed in children without physical signs of dehydration. It consists of following:

- Fluid therapy
- Continue feeding
- Zinc supplementation
- Identification of danger signs

Fluid therapy consists of treating the patients with home-available fluids. The mother should be educated to give, from the very first loose stool, increased amount of culturally appropriate, easily available fluids. Along with this, she is given ORS packets to use at home for prevention and treatment of dehydration (Table 7.15).

Warning Signs

The mother is instructed to return to the healthcare centre in the following conditions:

- High purge rate
- Persistent severe vomiting/frequent vomiting
- Marked thirst
- Refusal to drink and eat
- Blood in stool
- Fever
- Child not getting better within 3 days
- Rice watery stools—cholera

TABLE 7.15 Oral Rehydration Therapy to Prevent Dehydration (Plan A)

Age	Amount of ORS or Other Culturally Appropriate ORT Fluids to Give after Every Loose Stool	Amount of ORS to Provide for Use at Home
<24 months	50–100 mL /loose stool	500mL/day
2–10 years	100–200 mL/loose stool	1000 mL/day
10 years or above	As much as the child wants	2000 mL/day

If ORS is not available, home available fluids can be used.

TABLE 7.16 Amount of ORS to Be Used in First 4 hours for Children with Some Dehydration (Plan B)

Age	<4 months	4–11 months	12–23 months	2–4 years	5–14 years	>14 years
Approx. weight (kg)	<5	5–8	8–11	11–16	16–30	>30
ORS (in mL)	200–400	400–600	600–800	800–1200	1200–2200	>2200

If children want more ORS than given above, they should be allowed to take more. For local measure, use one glass (equal to 200 mL). Use the above table only when the weight of the child is not known. If the weight is known, give ORS at the rate of 75 mL/kg in first 4 hours.

- Anuria or failure to pass urine for >12 hours
- Altered sensorium, drowsiness, convulsions

Plan B—Treatment of Diarrhoea in Children with Some Dehydration

Children with some dehydration are given WHO ORS under supervision of a medical staff over 4 hours (Table 7.16). In infants and severely malnourished, dehydration should be corrected over 6 hours. For the replacement of ongoing losses, also give ORS 10–20 mL/kg for each loose stool. In infants below 6 months who are not breastfed, clear watery fluids are given along with ORS to prevent hypernatraemia. The child is reassessed at the end of 4 hours and managed accordingly. Breastfeeds are continued even during rehydration and semisolid foods are started after deficit replacement.

Plan C—Treatment of Diarrhoea in Children with Severe Dehydration

These children require immediate intravenous fluids as 100 mL/kg of the solution, either Ringer lactate (preferably) or normal saline (Table 7.17). In case of unavailability of IV line, the nasogastric tube can be used for rehydration by ORS. ORS is given at 20 mL/kg/hour (total 120 mL/kg) by nasogastric tube. If the child has abdominal distension or repeated vomitings, the nasogastric fluid is given more slowly. If the child is able to drink, ORS is given by mouth while the drip is being set up.

The various hydrating fluids available in the market are RL, 5% DNS, normal saline and acetated ringer. Ringer lactate is the fluid used initially for the correction of intracellular dehydration.

TABLE 7.17 Fluid Therapy in Severe Dehydration (Plan C)

Age	30 mL/kg*	70 mL/kg
<12 months	1 hours	5 hours
Older child	30 minutes	2½ hours

*Repeat once if radial pulse is weak or undetectable.

According to the age and clinical condition of the child 100 mL/kg of RL is given intravenously over 3–6 hours (Table 7.17). In severely malnourished or in infants, this amount is given slowly over 6 hours. The first 30 mL/kg is infused rapidly in first 1 hour. The remaining 70 mL/kg is infused in the next 5 hours (total 6 hours).

Reassess the child every 1–2 hours. If hydration status does not improve, give the IV drip more rapidly. Also give ORS 5 mL/kg/hour as soon as the child can drink, usually after 3–4 hours (infants) and 1–2 hours (children). Once the intracellular dehydration is corrected, Isolyte P can be used.

Reassess an infant after 6 hours and a child after 3 hours. Reclassify dehydration and manage accordingly (Plan A, B, C).

It is preferable to observe the child for at least 6 hours after rehydration to ensure that the mother is able to maintain the child's hydration status on ORS.

The child should be continuously assessed for urinary output, electrolytes, blood urea, serum creatinine and glucose levels. Monitor the vital signs and observe for complications (metabolic acidosis, etc.) and behavioural changes.

Give normal diet during the diarrhoeal episodes. As most of the cases in children are caused by rotavirus, antibiotics are not indicated in the children with loose stools.

Treatment of Complications in Acute Diarrhoea

1. *Hyponatraemia:* Sodium deficit can be calculated by the following formula:

$$\text{Sodium deficit} = (135 - \text{observed sodium}) \times \text{weight (kg)} \times 0.6$$

Part of this deficit should be corrected by using 3% saline until the sodium level raises to 125 mEq /L. Then the deficit should be corrected slowly over 24 hours.

2. *Hypokalaemia* (serum potassium <3.5 mEq /L): The concentration of potassium in the fluid can be increased by 20–40 mEq/L by adding potassium to the intravenous fluid and infused slowly. Transient, asymptomatic or mild hypokalaemia may spontaneously recover or may be treated with enteral potassium. Symptomatic or severe hypokalaemia should be corrected with a solution of intravenous potassium only when the urine output is good.
3. *Metabolic acidosis:* Metabolic acidosis gets corrected spontaneously with correction of dehydration. If the acidosis is severe (pH <7.25), sodium bicarbonate can be given. It is given as 1 mEq/kg IV over 1–2 minutes, followed by 0.5 mEq/kg IV every 10 minutes. Repeat for persistent severe metabolic acidosis. Further doses are given according to arterial blood gas analysis. The aim is to increase the plasma level to 18 mEq/L.

Maintenance

Maintenance fluid requirements are calculated as per the following formula, depending on the body weight:

Body weight (kg)	Amount of fluid to be given
Up to 10 kg	100 mL/kg
10–20 kg	1000 mL plus 50 mL/kg for each kg exceeding 10 kg
>20 kg	1500 mL plus 20 mL/kg for each kg exceeding 20 kg

Dietary Management

Dietary therapy has a key role in the treatment of diarrhoea. The child should continue to be fed a regular diet during diarrhoea contrary to the common belief that rest to the gut promotes early recovery. Continuation of feeding prevents or minimises the deterioration of nutritional status that normally accompanies such illness. Unnecessary starvation is detrimental to the recovery and leads to prolongation of diarrhoea.

1. *Breastfed infants:* In acute diarrhoea, breast feeding should be continued uninterrupted even during rehydration with ORS. Semisolid feeds should be started as soon as the deficit has been corrected.
2. *Non-breastfed infants:* In non-breastfed babies, milk, preferably mixed with cereals along with other semisolid foods, can be given during or after correction of dehydration. Milk should not be diluted with water during any phase of acute diarrhoea. One can use milk–cereal mixture, for example, milk–rice mixture.
3. *Older children:* Diet as appropriate for age is advised and consists of rice, khichri, pulses, curd, yoghurt, etc. Staple foods do not provide optimal calories per unit weight, and these should be enriched with fats and oils or sugar, for example, *khichri* with oil, rice with milk or curd and sugar, mashed banana with milk or curd and mashed potatoes with oil.

   Energy dense foods with the least bulk that are recommended for routine feeding and available in the household should be offered during diarrhoea, in small frequent aliquots, with *katori* and spoon.
4. *Role of lactose-free diet:* Lactose-free diet is recommended in very few infants suffering from acute diarrhoea. The indications are:
   - Prolonged or indeterminate diarrhoea
   - Progressive weight loss
   - >1% reducing substances in stools.
5. *Foods to be avoided:* Fruit juices, junk foods, spicy foods, carbonated fluids, sugar- and glucose-rich foods and foods with high fibre content; for example, coarse fruits and vegetables should be avoided.
6. *Feeding during recovery:* Nutrient dense foods should be given during recovery till the child reaches pre-illness weight or as expected for his age or height. This might take several weeks or longer, depending on the degree of deficit. An intake of at least 125% of normal RDA is advised during this period.
7. *Micronutrient in the treatment of diarrhoea:* Zinc, vitamin A, magnesium, selenium: zinc

therapy—zinc is advised in a dose of 10 mg/day in infants <6 months and 20 mg/day in children >6 months for a period of 2 weeks, as recommended by WHO and IAP. Zinc supplementation during diarrhoea promotes early recovery and improves immunity. It leads to 30% reduction in stool output. Its deficiency results in impaired maturation of enterocytes and hence defective tissue growth and repair.

Other Drugs in Diarrhoeal Disorders

1. *Antimotility drugs* such as loperamide are contraindicated as they cause stagnation of the fluids and give more time for harmful bacteria to multiply, thus prolonging the illness. They neither control the infection nor control the diarrhoea; rather they give a false impression of cure or well-being. Hence, these drugs are dangerous and may cause paralytic ileus, abdominal distension and sepsis.
2. *Adsorbents* such as kaolin and pectin should be avoided.
3. *Antisecretory agents:* Racecadotril is a new antisecretory agent. It can be given in a dose of 1.5 mg/kg every 8 hours, orally in secretory diarrhoea. It lowers stool output and decreases the duration of diarrhoea. The side effects are transient and may include nausea, vomiting, headache and constipation.
4. *Prebiotics and probiotics:* Discussed in detail later in this chapter
5. *Antibiotics:* These are not required in most cases of acute diarrhoea in children as they are mostly viral in origin. These were also not found to be useful in enterotoxigenic *E. coli* infections. They are used selectively in the following conditions:
   (a) Infections due to *Entamoeba histolytica*, *Shigella*, *Salmonella typhi*, *V. cholerae*, *G. lamblia*, *Y. enterocolitica*, *C. jejuni*, *S. aureus*, *C. difficile*, *B. cereus*, Enterobacteria, *Klebsiella* (Table 7.18)
   (b) Other factors
   - Associated extra gut infections such as pneumonias, septicaemia
   - Infants less than 3 months of age
   - Children with severe malnutrition (PEM Grade III and IV)

TABLE 7.18 Antibiotics Used in Diarrhoea

Infection	Antibiotics
Amoebiasis	Metronidazole
	Tinidazole
Shigellosis	Trimethoprim/sulphamethaoxazole
	Ampicillin
	Co-trimoxazole
	Nalidixic acid
Salmonella	Chloramphenicol
	Ciprofloxacin
	Co-trimoxazole
	Cefuroxime
	Ampicillin
	Gentamycin
	Ceftriaxone
Cholera	Tetracycline
	Doxycycline
	Erythromycin
	Trimethoprim/sulfamethoxazole
	Furazolidone
Giardiasis	Metronidazole
	Tinidazole
	Furazolidone
	Quinacrine
Y. enterocolitis	Tetracycline Gentamycin
Campylobacter	Erythromycin Tetracycline Oral neomycin Furazolidone
C. difficile	Vancomycin Metronidazole

Follow-Up

Once the loose stools are controlled, the patient should consume foods rich in calories and proteins for adequate weight gain. The mother should be educated regarding the following:

- Proper weaning practices
- Avoid bottle feeds
- Improve personal hygiene
- Use clean drinking water
- Proper food handling
- Hand washing
- Improved sanitation and toilet facilities
- Safe disposal of stools
- Immunisation (measles)

PREVENTION

1. *Diet:* Promote breastfeeding; exclusive breastfeeding up to 6 months, followed by complementary feeding.
2. *Hygiene:* Improved water and sanitary facilities; good hygiene should be maintained.
3. *Health education:* Hand washing; food preparation; inform about the early signs and symptoms of diarrhoea; details about the proper use of ORS.
4. *Immunisation:* Rotavirus vaccine and cholera vaccine can also be given.

NATIONAL DIARRHOEAL DISEASE CONTROL PROGRAMME

The Diarrhoeal Diseases Control Programme in India was started in 1978 to reduce mortality and morbidity due to diarrhoeal diseases. With the birth of the National Oral Rehydration Therapy (ORT) Programme in 1985–1986, the focus shifted to strengthening case management of diarrhoea for children under the age of 5 years and improving maternal knowledge related to the use of home available fluids, use of oral rehydration salt (ORS) solution and continued feeding. Ensuring availability of ORS packets at health facilities and in the community is an important aspect of the programme.

Supplies of ORS packets to the states are being organised by the central government. Twice a year, 150 packets of ORS are being supplied to all subcentres in the country as part of the drug kit. The programme emphasises the rational use of drugs for the management of diarrhoea. Adequate nutritional care of the child with diarrhoea and proper advice to mothers on feeding are two important areas of this programme. In 1992–1993, all programme activities were integrated with those of the CSSM programme. Since 1997, the programme has been integrated with the RCH programme.

PERSISTENT DIARRHOEA

It is defined as acute onset diarrhoea usually of infectious origin or postinfective sequelae like disaccharide intolerance which lasts for 14 days or more. It is usually associated with weight loss and extra gut infections. It is of two types:

1. Simple persistent diarrhoea—it responds to diet modification.
2. Persistent protracted diarrhoea—it is associated with weight loss and does not respond to diet modification.

PREDISPOSING FACTORS

The following factors predispose a child with acute diarrhoea to develop persistent diarrhoea:

- Malnutrition
- Immunocompromised child
- Extra gut infections such as pneumonia, urinary tract infections, septicaemia, HIV
- Parasitic infestation of the gut
- Improper treatment of acute diarrhoea

SIMPLE PERSISTENT DIARRHOEA

It lasts for ≥14 days, which responds to diet modification.

Aetiological Factors

- Infections by *G. lamblia*
- Agents that predispose to simple disaccharide intolerance

Features

- Healthy looking child without dehydration or toxic symptoms

- No weight loss
- Appetite preserved
- Perianal excoriation

Treatment

- Modification of diet like avoiding sugars in the diet
- Treatment of giardiasis/similar infestations

Prognosis

Prognosis is good.

PERSISTENT PROTRACTED DIARRHOEA

It lasts for ≥14 days, which does not respond to diet modification.

Aetiological Factors

- Infections—by bacteria, virus, fungi or parasites (Table 7.19). These may cause small-bowel bacterial over growth
- Postinfective sequelae like malabsorption (dietary protein intolerance)
- Extraintestinal infections such as UTI and chronic suppurative otitis media (CSOM)

Predisposing Factors

- Acute diarrhoea which has not been treated properly
- Protein energy malnutrition
- Lack of breastfeeding
- Bottle feeding
- Allergy to cow's milk
- Inappropriate use of antibiotics

TABLE 7.19 Etiological Factors for Persistent Protracted Diarrhoea

Bacteria	Virus	Fungi	Parasites
Shigella *Salmonella* Enteroadherent *E. coli*	HIV Herpes simplex CMV	*Candida albicans* *Cryptococcus neoformans*	*G. lamblia* *Cryptosporidium*

- Starvation during acute diarrhoeal disorders
- Vitamin A and zinc deficiency
- Extra intestinal infections

Clinical Features

It is common in malnourished and young children. Usual presenting features are

- loose stools and
- growth failure.

Persistent protracted diarrhoea is associated with malnutrition, infections and dehydration.

INVESTIGATIONS FOR PERSISTENT DIARRHOEA

1. Complete haemogram
2. Peripheral smear
3. Urine routine and culture
4. Blood culture—to detect persistent infection
5. Stool examination—leucocytosis, RBC, ova/cyst, pH, reducing substances, culture for *E. coli* (enteroaggregative), *Shigella*, *Salmonella*, *Cryptosporidium*
6. Serum proteins
7. HIV screening tests
8. Serum electrolytes
9. Tests for associated infections—X-ray chest
10. Therapeutic challenge tests for sugar, cow milk protein intolerance
11. Serology for amoebiasis—*Entamoeba histolytica* infection
12. Tissue diagnosis (wherever possible lymphnode, peritoneal or rectal mucosal biopsy, liver biopsy, etc.) for diseases like inflammatory bowel disease
13. Barium meal studies—contrast small-bowel study, large-bowel study (enema) to find out structure abnormalities surgical conditions and inflammatory bowel disease
14. Jejunal mucosal biopsy
    - Specific changes (lymphangiectasis, lymphoma, primary immunodeficiency, cow's milk protein intolerance)
    - Non-specific changes—diffuse or focal mucosal lesions of upper small intestines

15. Proctosigmoidoscopy—colitis
16. Sterile swab (rectum) for culture and sensitivity—infections
17. Screening for malabsorption
    - Faecal fat
    - D-xylose
    - Hydrogen breath test
    - Schillings test
18. Duodenal aspirate (bacterial colony count, culture and sensitivity)
19. Serum immunoglobulin—T- and B-cell functional defects (immune deficiency states)

Rare Selective but Definitive Tests

1. Pancreatic function tests for pancreatic exocrine enzyme deficiency
2. Liver function tests—for liver and biliary disorders
3. Sweat chloride test for cystic fibrosis
4. Disaccharidase enzyme assays (to assess intestinal damage)

MANAGEMENT

Treat dehydration according to its severity. The mainstay of treatment in persistent diarrhoea is dietary management. These patients should be treated in hospital setting.

1. Treat infections and associated conditions such as dyselectrolytemia and hypoglycaemia. Multivitamins, micronutrients, albumin transfusion, blood transfusion and immunoglobulins may also be given
2. Dietary management (Table 7.20)
   (a) Continue breastfeeding in a previously breastfed child
   (b) Diet—low-lactose diet (Plan A)
   (c) If there is no improvement in 2–3 days, change to lactose-free diet (Plan B)
   (d) Criteria for changing the plan from A to B or B to C:
      - Tendency for dehydration/reappearance of dehydration at any time
      - High purge volume
      - High purge rate—seven or more stools/day at the end of 7 days
      - Weight loss or poor weight gain in spite of taking 100 kcal/kg/day for last 3 days
   (e) Ideal sources for calories, proteins and fats
      - Carbohydrates—rice
      - Proteins—bengal gram, pulses groundnut, chicken and egg white
      - Fats—coconut oil due to high medium chain triglyceride content

TABLE 7.20 Dietary Management of Persistent Diarrhoea

Plan	Type of Diet	Contents of the Diet
A	Low milk/lactose diet	Rice, sugar, oil Cereal + milk Cereal + legume ± oil
B	Lactose free diet + low starch diet	Cereal based foods—rice, wheat, Bengal gram, ragi, sugar, oil Cereal + legume ± oil Egg white + cereal + sugar + oil
C	Lactose and sucrose free diet (monosaccharide based diet)	Glucose + oil + protein—egg/pureed chicken (monosaccharide based diet)

Indications for Antibiotics in Persistent Diarrhoea

- Neonates and young infants below 3 months
- Gross malnutrition
- Enteral infections due to invasive pathogens (such as Shigella, Salmonella), small-bowel bacterial overgrowth; protozoal diarrhoea (*Entamoeba histolytica, G. lamblia*), fungal diarrhoea
- Parenteral diarrhoea (diarrhoea due to infections such as urinary tract infections, respiratory tract infections, retrocardiac pneumonitis or septicaemia outside the gut)
- Positive parameters for occult sepsis
- Blood, mucus, pus cells (>10/Hpf) in the stools
- Immune deficiency states

Intravenous Parenteral Nutrition

In conditions where there is extensive damage to the intestinal mucosa or conditions where oral feeds are contraindicated, nutrients can be supplied through

TABLE 7.21 Constituents of Fluid for Partial Parenteral Nutrition

Constituents	Quantity (mL)
Maintenance fluid—isolyte P	250
25% dextrose	75
Amino acid solution	150
Sodium bicarbonate	18
KCl	5
Multivitamin infusion	2

500 mL will provide 300 calories. The above solution can be given as 50–75 mL/kg/day

parenteral route. The required calories and proteins are supplemented as a whole or partially.

Partial Parenteral Nutrition

The required calories and proteins are supplemented partially through parenteral route and partially through oral route (Table 7.21).

Total Parenteral Nutrition

The required calories and proteins are totally supplemented through parenteral route. Indications for TPN are as follows:

- Protracted diarrhoea with dehydration (>7 stools/day at the end of 7 days)
- Patients with intolerance to Plan C
- Weight loss or absence of weight gain after Plan C
- Severe form of inflammatory bowel disease
- Severe necrotising enterocolitis
- Persistent/protracted diarrhoea not tolerating oral feeds even after 10 days of treatment
- Enteroenteric fistulas
- Chronic diarrhoea with no weight gain
- Chronic diarrhoea where oral diet is contraindicated. Newborns with persistent diarrhoea in the postoperative period
- Severe forms of immune deficiency

Supplementation of Vitamins and Minerals

Vitamin A

Oral administration of a single dose of 1,00,000 IU for children below 1 year of age and 2,00,000 IU of vitamin A for children above the age of 1 year should be given routinely to all children who present with diarrhoea.

Zinc

A total of 10–20 mg/day of elemental zinc for children between 6 months and 3 years of age should be given.

Treatment Failure

The following features indicate treatment failure:

- Passage of >7 stools per day at the end of 7 days of treatment
- Weight loss or failure to gain weight in spite of taking a diet containing adequate calories and protein
- Development of oedema

Rehabilitation

The aim is to gain weight. This is done by means of health education and dietary advice. Calorie- and protein-rich food should be given.

PREVENTION

Following practices should be encouraged to prevent acute diarrhoea from developing into persistent diarrhoea:

- Promote breastfeeding up to 2 years
- Exclusive breastfeeding up to 6 months
- Continue feeding during diarrhoeal episodes
- Treatment of acute diarrhoea
- Use of rice-based ORS
- Health education—education regarding food safety
- Appropriate antibiotics

PROGNOSIS

If the condition presents at birth, the prognosis is bad. If it presents later, the prognosis is good. Factors associated with increased mortality in persistent diarrhoea are as follows:

- Respiratory infections
- Malnutrition

- Septicaemia
- Younger age

CHRONIC DIARRHOEA

Diarrhoea due to non-infective causes and lasting for more than 2 weeks duration is called chronic diarrhoea. It can occur in a previously normal child or in a child with inherited defects.

PREDISPOSING FACTORS

- Age <18 months
- Feeding practices—bottle feeding, lack of breast feeding and not feeding during an acute episode of diarrhoea
- Infections such as measles
- Malnutrition, vitamin A and zinc deficiency
- Poor hygiene
- Contamination of food
- Galactose malabsorption and intolerance to food

AETIOLOGY

The aetiology of chronic diarrhoeal disorders is as follows:

1. Malabsorption (defects in luminal phase, mucosal phase or transport phase)
   - Lactose intolerance
   - Inherited transport defect
   - Celiac disease
   - Glucose–galactose malabsorption
   - Bile salt malabsorption
   - Fat malabsorption
   - Enterokinase deficiency (severe protein malabsorption)
   - Cystic fibrosis
   - Congenital trypsinogen deficiency
   - Congenital enterokinase deficiency
2. Endocrine disorders
   - Hyperthyroidism
   - Carcinoid tumours
   - Addison's disease
   - Hypoparathyroidism
3. Anatomic defects
   - Short bowel syndrome
   - Congenital microvillus atrophy
   - Biliary atresia
   - Intestinal duplications
4. Metabolic disorders
   - Abetalipoproteinaemia
   - Acrodermatitis enteropathica
5. Pancreatic disorders
   - Chronic pancreatitis
   - Exocrine pancreatic deficiency
6. Inflammatory bowel disease
   - Crohn's disease
   - Ulcerative colitis
7. Nutritional causes
   - Pellagra
8. Neoplasms
   - VIP secreting tumours
   - Zollinger–Ellison syndrome
9. Chronic non-specific diarrhoea (irritable bowel syndrome)
   - Tropical sprue
10. Miscellaneous
    - Protein-losing enteropathy
    - Antibiotic-associated diarrhoea—*C. difficile*
    - Autoimmune enteropathy

In a child who presents with chronic diarrhoea, the cause of diarrhoea differs according to the age of the child. The common causes of diarrhoea in different age groups are given in Table 7.22.

CLASSIFICATION ON THE BASIS OF MECHANISM

I. *Osmotic diarrhoea:* Causes are as follows:
- Glucose–galactose malabsorption
- Disaccharides (lactase) absence or deficiency
- Laxative abuse (lactulose)
- Carbonated fluid excessive intake

II. *Secretory diarrhoea:* Causes are as follows:
- Infections—enterotoxigenic bacteria (toxins of *V. cholerae/E. coli*). These are the most common

TABLE 7.22 Common Causes of Chronic Diarrhoea in Different Age Groups

Age	Causes
Newborn	Congenital short bowel syndrome Neonatal lymphangiectasia Inherited transport defect like cystic fibrosis Glucose-galactose malabsorption Congenital chloridorrhoea Bile-salt malabsorption Milk enterocolitis Exocrine pancreatic deficiency Primary or secondary lymphangiectasia Hypo/abetalipoproteinaemia
1 months–2 years	Lactose intolerance, Cow's milk, soy and other allergies Celiac disease Irritable colon of infancy (chronic non-specific diarrhoea) Cystic fibrosis *C. difficile* (antibiotic-associated diarrhoea) VIP secreting tumours
Above 2 years	Celiac disease Inflammatory bowel disease Chronic non-specific diarrhoea (irritable bowel syndrome) Primary acquired lactase deficiency Tropical sprue Chronic pancreatitis/exocrine pancreatic deficiency Primary or secondary lymphangiectasia Hypo/abetalipoproteinaemia

causes of secretory diarrhoea. The toxins lead to failure of sodium pump, which is responsible for absorption of fluid in the gut

- Laxative abuse—anthraquinone cathartics and castor oil
- Drugs—quinine, colchicines and prostaglandins
- Bile acid malabsorption—terminal ileal disease
- Defective transport of sodium or chloride (congenital chloridorrhoea)
- Endocrine tumours—produce secretagogues. Examples are VIPoma (vasoactive intestinal peptide), Zollinger–Ellison syndrome (gastrin), carcinoid tumours (histamine, serotonin, polypeptide), medullary carcinoma of thyroid (calcitonin and prostaglandins), neuroblastoma

III. *Reduction of surface area of intestine*

- Small-bowel syndrome (postsurgery)
- Celiac disease

IV. *Motility disorders*

- Malnutrition
- Diabetes mellitus

INVESTIGATIONS

1. Stool examination for stool microscopy (leucocyte count, RBCs, ova, cysts and parasites), biochemistry (pH, reducing substances, occult blood), culture and sensitivities, stool osmotic gap and faecal fat estimation.
2. Blood tests are of limited value although peripheral blood eosinophilia may be present in children with food protein sensitivity. Investigation of immune function may reveal specific abnormalities. Measurement of renal function and electrolytes is particularly important in presence of poor fluid balance.
3. Radiological studies are rarely useful but barium meal and follow-through will exclude malrotation and may occasionally demonstrate a blind loop.
4. Endoscopy of the upper and lower gastrointestinal tracts, with biopsies, may be helpful.
5. Other tests such as endomysial antibodies, jejunal biopsy (celiac disease), sweat test (cystic fibrosis) for diagnosing specific conditions can also be done.

TREATMENT

The investigations and treatment are planned according to the type of diarrhoea and associated complaints.

ASSOCIATED CONDITIONS

Lactose Intolerance

Lactose intolerance is an inability to digest and absorb lactose (the sugar in milk) that results in gastrointestinal symptoms when milk or products containing milk are consumed. It may be primary or secondary:

- Primary—congenital absence of lactase enzyme

due to a mutation in the gene that is responsible for producing lactase.

- Secondary—more common, self-limiting. It is characterised by the destruction of microvilli, resulting in deficiency of lactase (which is present at tip of microvilli). As the new cells regenerate, the condition is corrected. The lactase enzyme is present in the newly regenerated cells.

Clinical Features

- Stable child with pain abdomen and flatulence
- Small stools
- Frequency—soon after the feeds
- Character of stools—soapy, syrupy and soundy
- Small-bowel sounds (borborygmi)
- Small-bowel colic—associated with colicky pain
- Sour taste
- Sore bottom (perianal excoriation due to acidic stools)

Investigations

1. Stool examination—the stools become normal once the food containing lactose is stopped.
   - Stool for reducing substances—positive
   - Stool pH—decreased
2. Oral tolerance test—lactose 2 g/kg is given orally. The rise in blood sugar <20 mg/dL goes in favour of lactose intolerance.
3. Hydrogen breath test—hydrogen excretion is measured after giving oral lactose 2 g/kg (maximum 50 g) with water after an overnight fast. In persons who are lactose intolerant, the lactose that is not digested and absorbed in the small intestine reaches the colon where the bacteria split the lactose into glucose and galactose and produce hydrogen (and/or methane) gas. Small amounts of the hydrogen and methane are absorbed from the colon into the blood and then travel to the lungs where they are excreted in the breath. Samples of breath are collected every 10 or 15 minutes for 3–5 hours after ingestion of the lactose, and are then analysed for hydrogen and/or methane. If hydrogen and/or methane in the breath is >20 ppm, it implies carbohydrate malabsorption.

Treatment

1. Diet management:
   - Primary lactose intolerance—these babies should be fed with lactose-free diet lifelong. Stop milk and products containing lactose.
   - Secondary lactose intolerance—milk and products containing lactose are stopped temporarily for few days. As the gut cells regenerate, these can be reintroduced.
2. Lactase enzyme—caplets or tablets of lactase are rarely available and can be taken with milk-containing foods.
3. Calcium and vitamin D supplements—these need to be given in cases of primary lactose intolerance since milk and its products are stopped lifelong.

Celiac Disease (Gluten-Sensitive Enteropathy)

It is an immune-mediated enteropathy in patients with genetic predisposition. There is permanent sensitivity to gluten and gluten-containing foods such as wheat, rye and barley. The gliadin fraction of the gluten is the active fraction and is responsible for celiac disease. The following are the features of this disease:

- Gluten-sensitive enteropathy
- Genetical predisposition, occurs in families
- Celiac disease develops after exposure to dietary wheat protein (gliadin), which causes sensitisation of lymphocytes in the lamina propria of the intestines
- T-cell-mediated mucosal damage
- Malabsorption occurs weeks to months after the introduction of foods containing the wheat protein

Pathology

Changes in the small bowel are villus atrophy, crypt hyperplasia and damage to the surface epithelium. The damage is more in the proximal bowel where the offending agents in the food enter. Due to the damage to the absorptive area, the digestive and absorptive capacity is decreased. There is remission after the offending agent is stopped.

Clinical Features

1. Gastrointestinal manifestations
   - Loss of appetite
   - Chronic diarrhoea with pale, loose and offensive stools
   - Abdominal distension, bloatedness and cramping (supposedly due to fermentative production of bowel gas)
   - Mouth ulcers
   - Vomiting
2. Non-gastrointestinal manifestations
   - Failure to thrive (weight loss and growth retardation)
   - Short stature
   - Pallor (anaemia)
   - Clubbing
   - Neurological symptoms—irritable, fretful and emotionally withdrawn
   - Abnormal coagulation due to vitamin K deficiency
3. Other associated features
   - IgA deficiency—increased risk of infections and autoimmune disease
   - Dermatitis herpetiformis
   - Pubertal delay in later childhood/growth failure
   - Hyposplenism (a small and underactive spleen)
   - Abnormal liver function tests (randomly detected on blood tests)
   - Dental enamel hypoplasia
   - Autoimmune disorders—diabetes mellitus type 1, autoimmune thyroiditis, primary biliary cirrhosis, etc.

Investigations

1. Serology
   - Anti-endomysium IgA antibodies (EMA)
   - Anti-tissue transglutaminase IgA antibody (TTG)

   These tests may be false-negative in children with IgA deficiency. Hence, it is important to measure the serum IgA levels prior to performing these tests
2. Intestinal biopsy—the biopsy should be repeated three times to diagnose this condition. First biopsy confirms the diagnosis and is suggestive of the following changes:
   - Partial or total villus atrophy
   - Crypt elongation
   - Decreased villus/crypt ratio
   - Intraepithelial lymphocytes will be increased with mitotic index >0.2%

   As the lesions are patchy, the biopsy may be normal. In such cases, it should be repeated at a different site. The second biopsy is done after 6 weeks of stopping the diet containing gluten to see if the changes are reversed. The third biopsy is repeated after giving a challenge diet with gluten and confirming that the changes reappear
3. Radiological studies show reduced bone mineral density due to associated nutritional deficiencies

Treatment

- Lifelong gluten-free diet is advised.
- Rice can be used instead of wheat, barley and rye.

Differential Diagnosis for Celiac Disease

Milk Protein Intolerance

- Common in children less than 2 years.
- Occurs within weeks after introducing cow's milk.
- Symptoms improve after milk is stopped.
- On reintroducing milk in the diet, the symptoms reappear within 3–4 days.
- Intestinal biopsy shows changes similar to celiac disease, but there are no changes after gluten challenge.

Prognosis of Celiac Disease

- The response to gluten-free diet starts within 1 week.
- The child may develop intestinal T-cell lymphoma or adenocarcinoma in the small intestine, pharynx or esophagus. Gluten-free diet started before the first year of life can be helpful in preventing the development of malignancies in later life.

ANTIBIOTIC-ASSOCIATED DIARRHOEA

It is unexplained diarrhoea which occurs between 2 hours and 2 months after starting antibiotics. It results from an imbalance in the colonic flora due to antibiotic therapy. This imbalance leads to malabsorption of carbohydrates and short-chain fatty acids leading to osmotic diarrhoea.

Pathogenesis

Use of antibiotics such as clindamycin eliminates the normal bacterial flora in the gut. This facilitates growth of other pathogenic bacteria such as *C. difficile* and *Clostridium* perfringes.

Treatment

Stop the offending agent and give supportive care. Most cases are usually mild and respond to this therapy. However, vancomycin can be given to treat *C. difficile*–induced diarrhoea if features of colitis are seen. Other drugs used in the treatment of antibiotic-associated diarrhoea are metronidazole and bacitracin.

Prognosis

Diarrhoea improves within 24–48 hours of stopping the offending drugs and starting the treatment.

Prevention

Probiotics and prebiotics can be used along with antibiotics to prevent antibiotic-associated diarrhoea.

PSEUDOMEMBRANOUS COLITIS

Pseudomembranous colitis is an acute inflammatory disease of the colon due to infection often caused by *C. difficile*, less frequently due to *Staphylococcus* species or enterotoxigenic *C. perfringens, Campylobacter* species, *Listeria* species and *Salmonella* species. In mild cases, there is minimal inflammation or oedema of the colonic mucosa. In more severe cases, the mucosa is covered with a loosely adherent membranous exudate (nodular or diffuse), hence the term pseudomembranous colitis. This condition is common after the intake of the following drugs:

- Clindamycin
- Cephalosporin
- Penicillin

Pathogenesis

Clindamycin and other broad-spectrum antibiotics cause alteration in the gut flora. Certain types of bacteria are killed, while few survive and multiply at a faster rate as there is less competition. *C. difficile* causes colonic mucositis by the production of toxins. These toxins are responsible for the development of pseudomembranous colitis and diarrhoea. This is more common in debilitating and postoperative patients.

Clinical Features

Symptoms appear 5–10 days after initiation of antibiotic therapy to even a few weeks after discontinuation of the antibiotic. They range from loose stools in the mildest cases to toxic megacolon (fever, nausea, vomiting and ileus) and colonic perforation (rigid abdomen and rebound tenderness) in the most severe cases. Symptoms include the following:

- Loose stools—profuse, watery or mucoid, green, foul smelling, may contain small amounts of blood
- Cramping abdominal pain
- Fever (usually 103°–105°F)
- Extraintestinal manifestations—oligoarthritis and iridocyclitis are extremely rare

Investigations

- Complete blood count—leucocytosis
- Stool examination—faecal leucocytes
- Serum proteins—hypoalbuminaemia
- CT scan abdomen—circumferential colonic wall thickening
- Endoscopy—punctuate yellow plaques in the colonic mucosa

Treatment

- Discontinue treatment with offending agents (clindamycin, cephalosporin, penicillin)
- Probiotics (sacchyromyces boulardii, lactobacillus)
- Bile acid sequestrants (cholestyramine)
- Intravenous immunoglobulins
- Antibiotic therapy with oral metronidazole or vancomycin for 10 days
- Surgical therapy in severe cases with toxic megacolon

Complications

- Toxic megacolon in severe cases

INFLAMMATORY BOWEL DISEASES

These include Crohn's disease and ulcerative colitis. There is inflammation of bowel in the absence of infections.

Crohn's Disease

It is characterised by patchy segmental transmural chronic inflammation of gut from oral cavity to anus. It can involve one segment or several segments with normal bowel in between them.

Clinical Features

- Non-specific—fever, anaemia, anorexia and weight loss
- Gastrointestinal manifestations—chronic diarrhoea, abdominal pain and tenderness, and perirectal fissures, fistulas and skin tags
- Extraintestinal manifestations—arthralgia, arthritis, uveitis, aphthous stomatitis, sacroiliitis and erythema nodosum.

Complications

- Sinus tracts to the skin
- Enteroenteric fistula
- Intestinal abscess

Investigations

1. Blood tests
   - Elevated white cell counts and sedimentation rates (infection or inflammation)
   - Low red blood cell counts (anaemia), low blood proteins and low body minerals, reflect loss of these elements due to chronic diarrhoea
   - Anti-saccharomyces cerevisiae antibodies are positive in approximately 50% of cases of Crohn's disease and hardly 5% cases of ulcerative colitis
2. Radiology
   (a) Plain X-ray abdomen may reveal any of the following—intestinal obstruction, bowel dilatation, narrowing of bowel lumen.
   (b) Single contrast upper gastrointestinal studies show decreased pliability of the distal stomach with severe narrowing of the body and antrum of the stomach with irregular ulcerated mucosal contours. The duodenal bulb also is involved and cannot be distinguished from the distal antrum (Ram's horn or Shofar sign). There are aphthous gastric ulcers or deep penetrating ulcers
   (c) Double contrast small intestinal series—findings in the small intestine:
   - Granularity due to oedema
   - Rose thorn appearance due to linear fissures
   - Spiculated appearance due to extensive ulceration
   - Separation of the bowels due to thickening of mesentery
   - String sign—narrowing of terminal ileum, due to oedema, fibrosis and spasm
   - Cobblestone appearance
   - Omega sign—due to concentric lesions

   (d) Double contrast barium enema—shows any of the following:
   - Skip lesions—discontinuous mucosal ulceration
   - Loss of haustrations
   - Narrowing of colon
   - Cobble-stone appearance due to linear and transverse ulceration
   - Anal fissures

(e) Coned-down view of terminal ileum from single-contrast barium enema—pseudopolyps is seen in this view

(f) Ultrasonogram
- Halo of submucosal oedema gives a target-like appearance (transversely) and double-track appearance (longitudinally)
- Bowel wall thickening
- Separation of bowel loops
- Bowel wall appears stiff with no peristalsis in the affected loop

(g) CT scan is helpful in diagnosing mesenteric thickening, lymphadenopathy, abscess formation, fistulas, luminal narrowing and stricture formation

3. Endoscopy reveals shallow aphthous gastric ulcers or deep penetrating ulcers; video capsule endoscopy can also be used for diagnosing Crohn's disease
4. Intestinal biopsy shows changes in the terminal ileum

Treatment

It consists of induction of remission and treatment of malnutrition. It includes the following:

- Prednisolone 2 mg/kg/day. The dose should be tapered as the disease becomes quiescent. The gradual tapering of dose can be done from 3 to 4 weeks of the initiation of treatment for several months. Maintenance therapy with prednisolone is not recommended
- Mesalamine 50–70 mg/kg/day (max. 3–4 g/day) for colitis
- Sulfasalazine 50–80 mg/kg/day in mild cases; no role in small-bowel disease
- 5-amino salicylic acid for mild-to-moderate colitis
- Immunomodulants—in severe cases, immunosuppressive drugs azathioprine, 6-mercaptopurine can be given
- Antibiotics—metronidazole
- Bile acid–binding agents
- Medium chain triglycerides
- Steroid dependent or refractory disease—methotrexate
- Surgical treatment—indications are intestinal obstruction, enteroenteric fistula, intestinal haemorrhage, intestinal perforation, failure of medical management and intestinal abscess

Prognosis

It depends on the site of involvement. Patients with small-bowel involvement have better prognosis than those with colon involvement. Incidence of colorectal carcinoma is high in patients of Crohn's disease.

Ulcerative Colitis

This is a condition characterised by recurrent bloody diarrhoea due to inflammation of colonic mucosa. It is usually seen in adolescence and childhood.

Etiopathogenesis

The cause is not known and is considered to be due to immunologically mediated reaction in people with genetic predisposition.

Sites Involved

Generally entire colon is affected. More common sites involved are large intestinal mucosa (rectum and distal colon).

Pathology

Inflammation is continuous and is limited to colonic mucosa. The following pathological changes are seen:

- Mucosa becomes friable
- Patchy ulceration; deeper ulceration with thickening of bowel wall
- Pseudopolyp formation due to regenerating mucosa
- Loss of colonic haustrations
- Tubular colon
- Inflammatory cell infiltrates in the lamina propria, distortion of crypt architecture, formation of crypt abscess and goblet cell depletion

Clinical Features

- Intestinal features—diarrhoea with blood and mucous, faecal urgency, tenesmus, colicky pain, lower abdominal pain relieved by defecation,

tenderness along the left side of the abdomen, increased bowel sounds.
- Non-specific features—high fever, prostration, anorexia with weight loss.
- Extraintestinal manifestations—arthralgia, arthritis, synovitis, ankylosing spondylitis, sacroiliitis, erythema nodosum, pyoderma gangrenosum, aphthous stomatitis, chronic active hepatitis, episcleritis, iritis, primary sclerosing cholangitis (PSC).

Grades of Clinical Severity

Depending on the stool frequency, abdominal tenderness, fever, degree of anaemia and hypoalbuminaemia, ulcerative colitis can present in the following ways:

1. *Prodromal pattern:* This type of presentation is not common. Clinical features are as follows:
   - Arthropathy
   - Erythema nodosum
   - Non-specific abdominal pain with minimal abdominal tenderness
   - Stool frequency increased
2. *Mild disease:* Clinical features are as follows:
   - Abdominal pain without systemic manifestations such as fever and tachycardia
   - Mild rectal bleeding
   - At least four bloody stools per day
3. Moderate disease: Clinical features are as follows:
   - At least five bloody stools per day
   - More rectal signs and symptoms apart from rectal bleeding and tenesmus
   - Colonic signs and symptoms—cramps, bloody diarrhoea, abdominal tenderness
4. Severe disease: It is associated with pancolitis. There will be more severe symptoms and more frequent exacerbations. Clinical features are as follows:
   - Stool frequency—six or more bloody stools per 2–4 hours
   - Dehydration
   - Anaemia
   - Profoundly toxic
   - Systemic symptoms—high fever, tachycardia
   - Marked abdominal tenderness with or without distension

Complications of Severe Disease

- Crypt abscess and fistula are less common than in Crohn's disease
- Pyoderma gangrenosum
- Iritis (pain and congestion of iris)
- Hepatitis (hepatomegaly and jaundice)
- Peripheral oedema due to excess protein loss
- Haemolytic anaemia
- Phelebitis

Investigations

- Haemoglobin—severe anaemia
- Elevated leucocytes in severe disease
- Acute phase reactants—ESR and CRP are elevated according to the disease activity
- Serum proteins—hypoalbuminaemia
- X-ray abdomen—reveals intestinal obstruction, bowel dilatation, loss of haustrations (pipe-stem appearance), shortening of bowel, pseudopolyps, ulcerations
- Intestinal biopsy—features of acute and chronic mucosal inflammation
- Barium enema may show a narrow, tubular, shortened colon with loss of haustral folds, pseudopolyps and small ulcers. It should not be done in a toxic mega colon. Diameter >6 cm measured radiologically suggests an increased risk for toxic megacolon. Backwash ileitis may be seen due to inflammatory reaction in the distal ileum
- Colonoscopy—microulcers and pseudopolyps; should be done with caution in severe disease to avoid the risk of perforation

Treatment

There is no medical cure to this condition. Treatment is supportive and aims to reduce inflammation and recurrences. Treatment includes the following:

1. Anti-inflammatory drugs are used in mild-to-moderate cases
2. Steroids—systemic administration (steroid enema for distal bowel involvement may also be done). Intravenous hydrocortisone can be given in severe cases
3. Sulfasalazine—50–80 mg/kg/day for severe disease. Mesalamine can also be given

4. Immunosuppressive drugs—may be used in severe cases; azathioprine and 6-mercaptopurine may be used
5. Broad-spectrum antibiotics
6. Nutritional support by parenteral nutrition
7. Surgical treatment is done for cases with severe complications. It includes proctocolectomy with ileostomy, or colectomy with rectal mucosectomy and endorectal pull through. Indications are:
   - Acute cases not responding to medical treatment
   - Intestinal obstruction/perforation
   - Uncontrolled bleeding or haemorrhage
   - Abscess (in the interloop or mesenteric regions)
   - Relapsing and remitting disease
   - Carcinoma
   - Fulminating disease
   - Fistula formation (enetroenteric, enterocolic, eneterocutaneous, rarely duodenocolic, entereovesical, colonovesical)

Prognosis

It is good for the cases of isolated distal colitis. However, follow-up may be needed in the following conditions:

- Toxic megacolon
- Adenocarcinoma in long-standing cases

Differentiating features of Crohn's disease and ulcerative colitis are given in Table 7.23.

ROLE OF DRUGS IN CHRONIC DIARRHOEA

Different drugs that can be used in case of chronic diarrhoea are summarised in Table 7.24.

RECOVERY CRITERIA FOR CHRONIC DIARRHOEA

- Less than three formed stools (after 2 months follow-up, the stools should not be watery or the number of stools should not be more than three times per day)

TABLE 7.23 Comparison of Features of Crohn's Disease and Ulcerative Colitis

Features	Crohn's Disease	Ulcerative Colitis
Clinical features		
Anorexia and loss of weight	More common	Less common
Abdominal pain	More severe, not relieved by bowel movement	Less severe, relieved by bowel movement
Abdominal mass	Commonly felt in the right lower quadrant	Not present
Sites involved	Affects small and large bowel; anal lesions are seen; stomach and esophagus may also be affected	Affects colonic mucosa only Rectum involved Perianal lesions are not seen
Ileal involvement	Common	Rare
Rectal involvement with bleeding	Rare	Common
Lesions	Skip lesions	Whole colon, (more common in rectum and distal colon); no skip lesions
Growth failure	+++	+
Pathology	Transmural disease Skip lesions Granuloma present Discrete ulcers in normal mucosa Cobblestone pattern of intestinal mucosa	Mucosa only involved Inflammation is continuous Granuloma may be present Large ulcer in the affected mucosa (Collar button ulcers) Lead pipe colon due to fibrosis
Investigations		
Plain X-ray	Frequently normal or non-specific Narrowing of bowel lumen Strictures	Loss of haustrations, shortening of bowel in severe cases Bowel wall oedema Luminal narrowing

(Table continued)

TABLE 7.23 *(Continued)*

Features	Crohn's Disease	Ulcerative Colitis
Contrast small-bowel study double contrast barium enema	Moulage sign—thickening of mucosal folds and effacement of mucosa Spiculated appearance Cobblestone appearance due to linear and transverse ulceration Rose thorn ulcers Pseudopolyps Severe luminal narrowing String sign—due to narrowing of the intestine due to oedema, fibrosis and spasm Fistulous tracts—enteroenteric fistulas	Mucosal granularity and oedema Ulceration Haustral thickening Pseudopolyposis Backwash ileitis (terminal ileum affected after total colon is affected) Colonic wall—stiff shortened, tubular Coned-down view—pseudopolyps will be seen in this view
Barium enema	Skip lesions	Contraindicated in toxic mega colon Loss of haustrations, Pseudopolyps Ulcerations, Shortening of bowel
Ultrasonogram	Thickening of bowel loops Separation of bowel loops Bull's eye appearance or target—like appearance (transversely) Double track appearance (longitudinally) Abscesses	Haustral thickening Presacral thickening Retroperitoneal fibrosis
Colonoscopy	Rectal sparing Colonic strictures	Colon stiff, shortened and tubular (lead pipe colon)

TABLE 7.24 Drugs in Chronic Diarrhoea

Conditions	Antibiotics	Doses	Duration
Non-infective diarrhoea			
Ulcerative colitis	Sulfasalazine	50–75 mg/kg/24 hour—in two to four divided doses	Continued even during remission
	Steroids Prednisolone	1–2 mg/kg/24 hour	3–4 months
Proctitis in ulcerative colitis	Aminosalicylate or hydrocortisone (100 mg) enema	Once a day at bed time	2–3 weeks
Antibiotic-associated diarrhoea -*C. difficile*	Vancomycin	40–50 mg/kg	7–14 days
Infective diarrhoea			
Amoebiasis—*E. histolytica*	Metronidazole	30–50 mg/kg	7–10 days
	Tinidazole	25 mg/kg	7 days
G. lamblia	Metronidazole	15–25 mg/kg	5 days
	Tinidazole	25 mg/kg	5 days
	Furazolidone	6 mg/kg	5 days
Enterotoxigenic and pathogenic *E. coli*	Co-trimoxazole	6–7 mg/kg of Trimethoprim—b.i.d.	5 days
Enteroinvasive *E. coli*	Trimethoprim—Co-trimoxazole	6–7 mg/kg of Trimethoprim—b.i.d.	5–7 days
Shigella	Trimethoprim—Co-trimoxazole	6–7 mg/kg—b.i.d.	5 days
	Nalidixic acid	50 mg/kg—tid	5 days
Salmonella Typhimurium	Chloramphenicol	50–80 mg/kg—b.i.d.	5 days
C. jejuni	Erythromycin	40 mg/kg—orally	5 days
Cholera	Tetracycline Doxycycline	50 mg/kg 6 mg/kg/day	3 days 3 days

(Table continued)

TABLE 7.24 *(Continued)*

Conditions	Antibiotics	Doses	Duration
C. difficile	Vancomycin	40 mg/kg/day	7–14 days
Septicaemia (based on antibiogram results)	Parenteral Ampicillin & garamycin	100 mg/kg/day in three divided doses 3–5 mg/kg/day in two divided doses	2–3 weeks
	Tobramycin	15 mg/kg	2–3 weeks
	Amikacin	15 mg/kg	2–3 weeks

- Three consecutive stool tests free from parasites and exudates
- Good tolerance to challenge tests with offending feeds
- Weight/height greater than 5th percentile on the local curve
- Haemoglobin more than 12 g/dL
- Haematocrit more than 35%
- Serum albumin more than 3 g/dL
- Serum iron-binding capacity normal
- Endoscopy—sigmoid colon and jejunal mucosal biopsy normal

PROTRACTED DIARRHOEA

It refers to chronic or persistent diarrhoea in a child when it results in malnutrition/failure to thrive. All the following features must be present in a child before labelling him as having protracted diarrhoea:

- Four or more liquid stools per day
- Duration of more than 14 days
- Sick infant with significant weight loss or failure to gain weight
- Diarrhoea refractory to conventional line of treatment

Protracted diarrhoea may be associated with the following features

- Protein energy malnutrition
- Micronutrient deficiencies
- Trace element deficiencies

TABLE 7.25 Aetiology of Protracted Diarrhoea

Classification	Causes
Nutritional	Malnutrition
Infective—enteral and extraenteral	Enteral—enteroinvasive *E. coli*, non-typhoid *Salmonella, Shigella, Cryptosporidium, Pseudomonas, C. albicans*, rotavirus Extraenteral—UTI, septicaemia, broncho-pneumonia
Infestations	Protozoa—giardiasis
Food factors	Monosaccharide intolerance Cow's milk protein intolerance Food sensitivity
Inborn errors of carbo-hydrate absorption	Glucose—galactose malabsorption
GIT causes	Celiac disease Congenital short bowel syndrome
Tumours	VIPoma (vasoactive intestinal peptide secreting tumour)
Miscellaneous	Idiopathic Cystic fibrosis Immunodeficiency

- Sepsis
- Immunodeficiency

Aetiological factors are listed in Table 7.25.

PATHOGENESIS

Protracted diarrhoea is characterised by structural damage to the villi, sepsis and consequent malabsorption. The factors associated with development of protracted diarrhoea are given in Table 7.26.

TABLE 7.26 Factors Associated with Protracted Diarrhoea

Types	Factors
Major factors	Malnutrition (macro- and micro-nutrients) Infections (enteral and non-enteral)
Minor factors	Absorption defects Food allergies Infestations Hypermotility Deconjugated bile acids Non-specific toxins

PATHOLOGY

There will be damage to the absorptive mucosal surface of small intestine. The damaged mucosa is either not repaired (impaired repair) or there is a delay in the repair of the damaged tissue. The reasons are as follows:

- Structural changes in the gut, leading to malabsorption of nutrients
- Intolerance to nutrients
- Allergy to cow's milk protein or wheat protein
- Small-bowel overgrowth
- Alteration in the intestinal normal flora

CLINICAL FEATURES

They may vary from mild to severe:

- Diarrhoea for more than 14 days
- Weight loss
- Severely malnourished
- Sick-looking child
- Signs of nutritional deficiency

INVESTIGATIONS

1. Complete blood count with ESR and peripheral smear
   - Total and differential count—eosinophils will be increased in food protein sensitivity
   - Haematocrit
   - ESR
   - Reticulocyte count
   - Smear for malarial parasites
2. Liver function tests
   - Serum proteins—total/albumin/globulin
   - Serum bilirubin—total/direct/indirect
   - Serum enzymes—SGOT/SGPT/alkaline phosphatase/gamma glutamyl transferase
3. Stool examination
   - Macroscopic examination
   - Microscopic examination
   - pH is acidic in lactose intolerance
   - Stool electrolytes
   - Stool osmolality is helpful in differentiating between osmotic and secretory diarrhoea
   - Stool for reducing substances >1% in lactose intolerance
   - Stool culture—helps identify the causative organism—for *Salmonella* and *Shigella* should be done
4. X-ray chest—for evidence of bronchopneumonia, tuberculosis
5. X-ray abdomen
   - Erect posture—to see for air under the diaphragm
   - Barium meal examination (malrotation, blind loop syndrome)

When the patient is severely dehydrated, do the following tests:

1. Renal function tests—blood urea/creatinine
2. Serum electrolyte estimation
3. Blood gas estimations

INVESTIGATIONS FOR SPECIFIC CONDITIONS

- Tests for malabsorption—stools from reducing substances (lactose intolerance), stool fat estimation (fat malabsorption)
- Tests for cystic fibrosis—sweat test
- Jejunal biopsy
- Chromatography of fresh stool for inborn errors of metabolism
- Serum for gut autoantibody
- Gut hormones
- Serum and urine for toxin (food poisoning)
- Gut endoscopy

TREATMENT

Treatment consists of the following phases:

1. Resuscitation phase (within 48 hours)
2. Control-of-diarrhoea phase (2–5 days)
3. Rehabilitation phase (5 days to 8–10 weeks)—rapid restoration of wasted tissues (Table 7.27)

TABLE 7.27 Treatment of Severe Form of Protracted Diarrhoea

Phases	Duration of Treatment	Aim of Management	Steps in Management
Phase I (resuscitative phase)	<48 hours	Resuscitation	Correction of shock Correction of dehydration Correction of dyselectrolytemia Treat hypoglycaemia, hypothermia, vitamin deficiencies Correct azotemia Treatment of fulminant sepsis Treatment of hypoproteinaemia and anaemia
Phase II (diarrhoea control phase)	2–5 days	Control of diarrhoea	At least partial control of diarrhoea GMC regimen for bowel sterilisation Amino acid infusion
Phase III (phase of oral realimentation or phase of rehabilitation)	5 days to 8–10 weeks	Nutritional rehabilitation	Improve general health Correct nutritional deficiencies Catch up growth Health education Shift the child to regular diet

Phase I—Resuscitation Phase

1. Management of dehydration and shock with intravenous fluids
2. Electrolyte imbalance—potassium chloride should be added in the intravenous fluids; hyponatraemia should be corrected with hypertonic saline
3. Sepsis—broad-spectrum antibiotics
4. Anaemia—packed cell transfusion
5. Hypoproteinaemia can be treated with amino-acid infusion
6. Renal shutdown should be treated with diuretics. If there is no response, consider dialysis
7. Monitoring of the child with daily weight; vital signs should be done
8. Cross-matching of blood for emergency blood transfusion, if required
9. Barrier nursing—as these children are prone to get infected, strict asepsis should be followed

Phase II—Diarrhoea Control Phase

1. Control of diarrhoea (at least partially)
   - Sepsis control (local and systemic)
   - Nutritional support
   - Drugs
2. GMC regimen for bowel sterilisation should be started once partial control of diarrhoea is achieved. This is given below:
   - Gentamycin—orally 30 mg/kg/day in three divided doses
   - Metronidazole—25 mg/kg/day in three divided doses
   - Cholesteramine—orally 200–300 mg/kg/day
3. Nutritional support (parenteral or combined oral and parenteral)—nutritional supplementation should be given. Total parenteral nutrition can be given in severe cases

Phase III—Phase of Rehabilitation

1. Once there is a partial control of diarrhoea within 3–4 days of starting the treatment, oral fluids should be started. Initially small feeds of non-lactose-containing fluids with high energy are given. Non-lactose non-sucrose formulas also can be given. Realimentation can cause vomiting or food intolerance, electrolyte imbalance and dehydration. The child should be slowly shifted from the intravenous fluids to regular diet.
2. Health education—the parents and the child should be educated about the food preparation and hygiene.

MONITORING

- Monitor weight
- Serum protein

- Haemoglobin
- Electrolytes
- Glucose
- Blood urea
- Serum creatinine

FOLLOW-UP

The child should be called for regular follow-ups, so that any recurrence of diarrhoea can be treated early.

PROGNOSIS

The mortality rate with early treatment is about 5%.

Differences between persistent and protracted diarrhoea are given in Table 7.28.

TABLE 7.28 Differences between Persistent Diarrhoea and Protracted Diarrhoea

Features	Persistent Diarrhoea	Protracted Diarrhoea
Appearance	Healthy	Ill looking
Appetite	Present	Absent
Signs of dehydration	Absent	Present
Malnutrition	Absent	Present
Infection	Absent	Present
Weight loss	Absent	Present
Structural damage to the villi	Absent	Present
Associated conditions	Enzyme deficiencies—simple disaccharide intolerance	Severe sepsis Mucosal damage

PROBIOTICS AND PREBIOTICS

NORMAL GUT FLORA

The gut of a newborn baby is sterile at birth. Later, it gets colonised by organisms in the surrounding environment. The flora present in the gut consists of commensal organisms which do not cause any disease. These are as follows:

- Bacteroides
- Fusobacterium
- Peptostreptococcus
- *E. coli*
- Lactobacillus acidophilus
- fungi—Saccharomyces, Aspergillus

Advantages of Gut Flora

The advantages of normal gut flora are as follows:

- Forms a barrier against harmful pathogenic bacteria.
- Produces lactic acid and fatty acids that lower the gut pH.
- Aids in digestion, promotes assimilation and absorption of food.
- Promotes development of gut immunity and augments the host's ability to resist infections.
- Produces short-chain fatty acids which control the intestinal epithelial cell differentiation.
- Plays a role in metabolising dietary carcinogens.
- Prevents development of inflammatory bowel diseases.

Disadvantages

The gut flora produces certain toxic substances which are harmful to health.

PROBIOTICS

The viability of live bacteria in food products during transit in the gut may be altered. Hence, the concept of probiotics was designed. Probiotics are defined as living microorganisms that confer a health benefit on the host by improving its intestinal microbial balance when consumed in adequate amounts. Their characteristic features are as follows:

- They are live microbial feed supplements
- They compete with the pathogens for micronutrients
- They are naturally colonised in the human gut
- They are safe with no pathogenic side effects
- They are able to survive in gastrointestinal tract with beneficial effects

Intestinal organisms used as probiotics

Bacteria	Fungi
Lactic acid-producing bacteria • Lactobacilli: *L. acidophilus*, • Lactococci: *L. lactis*, • Bifidobacteria: *B. bifidum* • *Streptococcus thermophilus* *Bacillus* species: *B. subtilis* *E. coli* strain nissle	*Saccharomyces boulardii* *Saccharomyces cerevisiae*

Dairy-based foods act as a major source of probiotics in food. They contain lactobacilli and bifidobacteria which are important members of the gut microflora.

Beneficial Effects

- Increase resistance to infectious diseases of the intestine—diarrhoea, colitis, gastroenteritis, rotavirus infection, etc.
- Decrease duration of diarrhoea and decrease flatulence
- Improve digestion
- Correct lactose intolerance and poor utilisation of food nutrients
- Act as an anti-constipation factor
- Synthesis of vitamins such as biotin and vitamin K
- Aid absorption of minerals especially calcium and magnesium due to increased intestinal acidity

Role in Lactose Tolerance

Probiotics improve the digestibility of lactose in patients with lactose intolerance. This occurs due to any of the following:

- Lactase activity of the probiotic bacteria
- Stimulation of the host's mucosal lactase activity

Effect on Host Microorganisms

Probiotics improve the colonisation of gut with useful microorganisms. They also increase their resistance to pathogenic organisms by the following mechanisms:

1. Production of strong acids (lactic acid bacilli lower the colon pH and inhibit the growth of harmful bacteria such as *E. coli*, *Clostridium*, *Salmonella* and *Shigella*). Lactic acid can suppress formation of cancer-causing amines and cancer-promoting enzymes in the intestine.
2. Metabolising toxins, thus accelerating the breakdown of organic waste.
3. Fragmenting and decreasing sludge build-up and preventing dangerous concentration of sulfide, nitrite, ammonia and various organic acids in the intestines.
4. Producing a wide variety of antibiotic substances (acidophilin, bacteriocin, etc.) which control the level of pathogenic bacteria and fungi such as *Candida*.
5. Occupying potential colonisation sites and dislodging harmful bacteria from the large intestine. This happens when these microorganisms are present in abundance. They normalise the bowel function in chronic constipation.

Effect on Pathogenic Microorganisms

They inhibit the adhesion of the pathogens to the intestinal epithelial cells by

- modification of toxins;
- modification of toxin receptors;
- enhanced immune response to pathogens;
- production of antimicrobial substances.

PREBIOTICS

They are non-digestible food stuffs that selectively stimulate the growth and activity of beneficial bacteria in the gut. These are nutrients that are used by specific bacteria and that can be added to the diet to increase the chances of these particular bacteria growing and thriving in the intestine. They promote the proliferation of bifido bacteria in the colon.

The examples of prebiotics include fructo- and galacto-oligosaccharides, inulin, lactulose, lactitol, etc. Oligosaccharides which are resistant to digestion reach the colon and promote the growth of probiotic, bifidogenic bacterial strains. Fructo-oligosaccharides (FOS) are fructose sugar molecules linked together in long chains which are naturally seen in banana, garlic, onions, honey, barley, wheat and rye. Prebiotics may have a role in immune stimulation, as evidenced

by decreased incidence and duration of diarrhoea, fever and cold in children who were supplemented with prebiotics.

SYNBIOTICS

As probiotics are mainly active in the small intestine and prebiotics are only effective in the large intestine, the combination of the two may give a synergistic effect. This has given rise to the concept of 'Synbiotics'. These are also known as health-enhancing or health-promoting 'functional food'.

Advantages of synbiotics are as follows:

- Anticarcinogenic
- Antimicrobial activity prevents colonisation by pathogenic microbials
- Anti-diarrhoeal activity
- Antiallergogenic
- Immunomodulation
- Decrease lipid level
- Help decrease blood glucose levels
- Anti-osteoporotic activity
- Improve mineral absorption
- Suppress the putrefactive process in the stomach

Differences between probiotics, prebiotics and synbiotics are given in Table 7.29.

TABLE 7.29 Probiotics, Prebiotics and Synbiotics

Types	Constituents and Action	Examples
Probiotics	Dietary supplement of living bacteria Probiotics improve the colonisation of useful microorganisms and also their resistance	*Lactobacillus* Bifidobacteria *S. boulardii*
Prebiotics	Dietary supplements of substrates preferentially fermented by gut bacteria; they stimulate the growth and activity of beneficial bacteria in the gut	Fructo-oligosaccharides Galacto-oligosaccharides Lactulose Lactitol
Synbiotics	Combination of probiotics and prebiotics	Bifidobacteria plus fructo-oligosaccharides *Lactobacillus* and inulins *Lactobacillus* plus fructo-oligosaccharides Bifidobacteria with inulins

CHAPTER 8

Disorders of Cardiovascular System

Cardiovascular disorders are very common in children. A detailed history is the basis of correct diagnosis. Early diagnosis and intervention prevents complications due to such disorders. Maternal history of infections such as rubella or intake of teratogenic drugs is helpful in the diagnosis of congenital heart disorders. A detailed family history for cardiac disorders is necessary as some of the disorders recur in family members.

HISTORY TAKING

History taking in children with suspected cardiac disorders is given below:

Age

- Congenital heart diseases such as ventricular septal defect (VSD), patent ductus arteriosus (PDA) and tetralogy of Fallot (TOF) usually present in the early infancy. The age of presentation varies from birth to first few years of life depending on the severity of the condition.
- Atrial septal defect, although present since birth, usually presents during adolescence or adulthood.
- Rheumatic fever is common in the age group of 5–15 years, so rheumatic heart disease (RHD) occurs after the age of 5 years.

Sex

Atrial septal defect is common in females.

Place

Incidence of PDA is high in people living at high altitudes.

Presenting Complaints

The examiner should record the presenting complaints in the informant's/patient's own words. The onset of symptoms should always be recorded in the chronological order of their appearance.

Example of presenting complaints in chronological order of appearance

- Cough—10 days
- Fever—9 days
- Difficulty in breathing—5 days

The usual presenting complaints in a cardiac case are as follows:

- Increased precordial activity
- Failure to thrive
- Cyanosis
- Difficulty in breathing
- Cough
- Recurrent lower respiratory infections

- Joint pains

The following symptoms should be enquired in an older child:

- Cyanosis
- Exercise intolerance
- Difficulty in breathing
- Chest pain

History of Present Illness

This comprises the details of the presenting complaints in chronological order. This is followed by a detailed clinical examination, which will help to reach a diagnosis.

Features of Cardiovascular System Disorders

Hyperpnoea. Increased respiration without awareness.

Dyspnoea. Unpleasant awareness of one's own breathing. Types of dyspnoea are described based on the position in which the patient develops dyspnoea (Table 8.1). Grading of dyspnoea is done by the New York Heart Association (NYHA) based on limitation of activities in a patient with underlying heart disease (Table 8.2).

1. *Orthopnoea*: Dyspnoea develops in recumbent position and is relieved by sitting.

TABLE 8.1 Types of Dyspnoea and Causative Factors

Type	Features	Conditions
Orthopnoea	Dyspnoea in supine posture	Cardiac failure
Trepopnoea	Dyspnoea in lateral decubitus	Pleural effusion
Platypnoea	Dyspnoea in sitting posture	Left atrial myxomas, left atrial thrombus, pulmonary arteriovenous fistula
Exertional dyspnoea	Dyspnoea on exertion	Cardiac failure, anaemia
PND	Dyspnoea in the midnight. It usually occurs at night.	Acute left ventricular failure

PND—paroxysmal nocturnal dyspnoea.

TABLE 8.2 Grading of Dyspnoea by NYHA

Grades	Features
I	No limitation during ordinary activity
II	Slight limitation during ordinary activity
III	Marked limitation of normal activities with no symptoms at rest
IV	Dyspnoea at rest

Mechanism—there is an increase in venous return on lying down due to redistribution of blood from the legs. A compensated heart is not able to pump this extra volume. This results in pulmonary congestion. This leads to decreased pulmonary compliance. Also, the diaphragm is elevated on lying down, thus decreasing the lung volume. All these factors contribute to the development of dyspnoea in lying down posture in a patient of cardiac failure.

2. *Trepopnoea:* Dyspnoea occurs on lying down in lateral decubitus position (right or left lateral decubitus position).

   Mechanism—in patients with left-sided pleural effusion, when the patient lies down on the right side, the fluid pushes the lung on the normal side. This leads to dyspnoea. The patient feels better on lying on the left side in case of left-sided pleural effusion.
3. *Platypnoea:* Dyspnoea occurs only when the patient is sitting in an upright position.

   Causes

   - Left atrial myxomas
   - Left atrial thrombus
   - Pulmonary arteriovenous fistula
4. *Exertional dyspnoea:* Dyspnoea occurs after exertion. This is seen in left ventricular failure.
5. *Paroxysmal nocturnal dyspnoea (PND):* It is otherwise known as *cardiac asthma* or *air hunger*. All of a sudden at midnight while the patient is in deep sleep, he becomes severely dyspnoeic with cough and wheezing and is forced to get up from the bed. He walks and goes to the window. The dyspnoea is relieved after few minutes by standing upright.

   Cause—acute left ventricular failure.

Mechanism

- Increased venous return in recumbent posture due to resorption of oedematous fluid. There is collection of fluid in the dependent parts of the body in standing position during the day. On lying down, this fluid moves to the lungs and increases the pulmonary blood volume. This leads to frank pulmonary oedema. This redistribution of fluid takes 2–4 hours to increase the left atrial pressure. It takes 10–30 minutes subsequently to redistribute the fluid back into the tissues. This is achieved by gravitational pooling of blood on standing upright.
- Reduction of vital capacity in the supine position. Diaphragm is raised due to increased intra-abdominal pressure.
- Reduced adrenergic drive during sleep results in withdrawal of adrenergic effect. This decreases the left ventricular contraction during sleep.
- Depressed respiratory centre.
- Mobilisation of the oedema fluid from extravascular to intravascular compartment in the supine position.

Palpitation. It is the sensation of one's own rapid or forceful heartbeat. The causes are as follows:

1. Extra systoles
2. Tachyarrythmias
3. Endocrine causes
   - Pheochromocytoma
   - Thyrotoxicosis
   - Hypoglycaemia
4. High output state
   - Anaemia
   - Fever
   - Anxiety
5. Drugs
   - Sympathomimetics
   - Vasodilators
   - Atropine
6. Idiopathic

Chest Pain. Chest pain is a symptom which occurs in older children and adolescents mostly due to non-cardiac causes. The following questions should be asked to evaluate if the chest pain is cardiac in origin:

- Nature of pain—is it stabbing or squeezing?
- Aggravating factors—is the pain activity related to or aggravated by exertion.
- Relieving factors—is the pain relieved by rest?
- Radiation—does the pain radiate to other parts of body such as neck or left shoulders and arms?
- Duration of pain.
- Accompanying features—is the pain accompanied by syncope or palpitations?

Oedema. Oedema occurs in children with right ventricular failure as the blood from superior and inferior vena cava is not effectively pumped to the lungs. This results in tender hepatomegaly and pedal/sacral oedema.

Syncope. It is a sudden, transient loss of consciousness due to impairment of cerebral blood flow. It occurs due to decreased cardiac output and has thromboembolic manifestations.

Haemoptysis. It is a condition where blood is coughed up. The blood may be seen alone or along with sputum. It is seen in cardiac conditions such as mitral stenosis (MS).

Cough. In left ventricular failure, there is pooling of blood in left atrium (LA). This results in increased left atrial pressure which leads to increase in pulmonary venous pressure and pulmonary congestion. This results in cough.

Oliguria. In left ventricular failure, the cardiac output is decreased. This results in decreased renal blood flow, which in turn decreases the glomerular filtration rate (GFR). Thus the urine output is decreased.

Fatigue and Tiredness. These occur in children with decreased cardiac output.

Recurrent Respiratory Tract Infections. Children with more than six infections in a year, with each infection lasting for at least a week, should be treated in a hospital. Recurrent respiratory tract infections occur due to pulmonary congestion as occurs in congenital heart diseases with left-to-right shunts. The following history should be asked in such cases:

- Number of episodes per month
- Severity
- Whether associated with fever or not
- Hospitalisation/treatment

Cyanosis. It occurs in children with right-to-left shunts.

Specific Disease Aetiology

1. Rheumatic fever (licks the joint, bites the heart and kicks the brain)

- Sore throat
- Fever
- Epistaxis
- Fleeting pain and swelling of the major joints due to arthritis (migratory polyarthritis)
- Chest pain
- Involuntary movements (chorea)

2. Cyanotic heart disease

- Cyanosis—bluish discolouration of the body
- Cyanotic spells—onset, sites involved (central/peripheral), aggravating/relieving factors
- Squatting/squatting equivalents—is seen in children with TOF
- Increase in severity of cyanosis
- Difficulty in breathing

Complications of Heart Disease

History suggestive of complications of heart disease should be taken as follows:

1. *Failure to thrive:* Inadequate weight gain/loss of weight is seen in chronic cases with failure as they spend more energy for increased respiratory rate and tachycardia. (In acute stages of congestive cardiac failure, there is weight gain.) Delay in growth and development may be seen
2. *Cardiac failure:* The important points in history that should be noted in a child with cardiac failure are as follows:
   (a) Dyspnoea
      - Duration
      - Grading—at the onset
      - Aggravating/relieving factors
      - Improving/deteriorating
      - Orthopnoea
      - Fatigue
      - Cough

   (b) Chest pain
   (c) Oliguria
   (d) Oedema of legs/back, pedal oedema, facial puffiness
   (e) Pain in abdomen due to tender hepatomegaly
3. *Infective endocarditis:* The important points in history that should be noted in a child with infective endocarditis are as follows:
   (a) Prolonged fever with chills and rigours
   (b) Purpura
   (c) Pain at finger ends
   (d) Arthralgia
   (e) Fatigue
4. *Thromboembolic manifestations:* A child with thromboembolic manifestations may present with any of the following:
   (a) Visual disturbances and blackouts
   (b) Convulsions
   (c) Neurological deficits
   (d) Syncope
5. *Renal symptoms:* The renal symptoms are oliguria and nocturia
6. *Left atrial enlargement:* Left atrial enlargement in mitral stenosis can press over the recurrent laryngeal nerve and cause hoarseness of voice. Dilated aortic aneurysm can also cause similar symptoms

Complications of Cyanotic Heart Disease

History related to complications of cyanotic heart disease is as follows:

- Plethora due to polycythaemia
- Bleeding episodes
- Fever (brain abscess)
- Incessant crying, altered sensorium, convulsions, headache, focal neurological defects due to brain abscess/infarction
- Painful swelling of the joints (gout)
- Abdominal pain due to congestive gastropathy (congestion of stomach seen in patients with cardiac failure), mesenteric embolism and tender hepatomegaly

History of Past Illness

- Rheumatic fever
- Kawasaki's disease (associated with myocardial ischaemia in children)
- Chaga's disease (associated with dilated cardiomyopathy).

Antenatal History

The following questions should be asked from the mother if the child is suffering from any congenital heart disease.

- Was the pregnancy booked/unbooked?
- Was the mother immunised for rubella prior to delivery?
- Was the mother scanned in the antenatal period? (Foetal ultrasonogram examination to rule out congenital defects in the heart and microcephaly as these may be associated with congenital rubella.)

Intrauterine Infection and Teratogenic Drug Intake

It is important for the clinician to enquire into the possible causes leading to congenital heart defect in the child. The reason often lies in the periconceptional period, especially the first trimester, wherein the foetus may have been exposed to various intrauterine infections (Table 8.3) or teratogenic drugs (Greek: *teratos*—monster, *genes*—born) (Table 8.4).

TABLE 8.3 Intrauterine Infections and Its Effect on the Foetus

Intrauterine Infection	Cardiac Defects
Rubella	Pulmonary artery stenosis, patent ductus arteriosus, ventricular septal defect, atrial septal defect
Mumps	Endocardial fibroelastosis

History suggestive of TORCH infection:

- Fever with rash in the first trimester may be suggestive of rubella. Maternal rubella leads to congenital heart diseases such as PDA and VSD in the child.
- Painful swelling behind the ears may be due to postauricular lymphadenopathy in patients with rubella infection.

Maternal Conditions

History of other maternal conditions which

TABLE 8.4 Teratogenic Drugs and Their Effect on the Foetus

Drugs	Cardiac Defects	Other Features
Sodium valproate	CoA, hypoplastic left heart, AS, pulmonary atresia, VSD	Facial dysmorphism, learning disability, motor incoordination
Hydantoin	PS, VSD, ASD, PDA, COA	Nail hypoplasia, growth retardation
Alcohol	VSD, PDA, ASD, and TOF	Growth retardation, mental retardation, microcephaly, flexion contractures
Trimethadione	TGA, TOF, Hypoplastic left heart syndrome	Growth retardation, synophrys, low set ears, genital anomalies
Oestrogen	VSD, TOF, TGA	Ambiguous genitalia
Progesterone	TOF	Ambiguous genitalia
Thalidomide	TOF, VSD, ASD, truncus arteriosus	Limb anomalies, absent external ear, duodenal atresia, anal atresia
Lithium	ASD, Ebstein's anomaly	Hypotonia, limb anomalies, gastrointestinal tract anomalies
Amphetamines	VSD, PDA, ASD, TGA, TOF	Learning disability, motor incoordination
Indomethacin	Intrauterine closure of ductus arteriosus	Renal dysfunction
Vitamin D	Supravalvular aortic stenosis	Craniosynostosis
Vitamin A	Conotruncal anomalies, TOF, pulmonary atresia, truncus arteriosus, TGA	Abnormal facies, neural and renal anomalies

AS—aortic stenosis, ASD—atrial septal defect, CoA—coarctation of aorta, PDA—patent ductus arteriosus, PS—pulmonary stenosis, TGA—transposition of great arteries, TOF—tetralogy of Fallot, VSD—ventricular septal defect; conotruncal anomalies—defect in separation of aorta and pulmonay artery by the spiral septum results in conditions such as truncus arteriosus.

TABLE 8.5 Maternal Conditions and Associated Cardiac Defects in the Child

Maternal Conditions	Heart Defects in the Child
Diabetes	Structural defects—TGA, VSD, PDA HOCM Conotruncal anomalies
SLE	Congenital heart block
Phenylketonuria	TOF, VSD, ASD, PDA, COA

ASD—atrial septal defect, COA—coarctation of aorta, HOCM—hypertrophic abstructive cardiomyopathy, PDA—patent ductus arteriosus, SLE—systemic lupus erythematosus, TGA—transposition of great arteries, TOF—tetralogy of Fallot, VSD—ventricular septal defect.

predispose to cardiac disorders in infants should be taken as given below:

1. *Maternal diseases:* Risk for congenital heart disease is high if the mother suffers from conditions such as diabetes, hypertension, systemic lupus erythematosus (SLE) and phenylketonuria (Table 8.5).
2. *Irradiation:* The maximum permissible limit of radiations is 500 millirads during the entire period of pregnancy. More than 500 millirads of radiation in early pregnancy can lead to cardiac defects. More than 10,000 millirads causes abortion.
3. *Nutrition:* Maternal malnutrition predisposes to cardiac defects in the baby.

Birth History

Important events that take place during the birth of a child must be noted.

1. Full term/preterm (preterm babies have a high incidence of PDA)
2. Mode of delivery
3. Birth asphyxia—cry immediate/delayed
4. Birth weight
   - Low birth weight is commonly seen in babies having congenital heart disease. For instance, intrauterine growth retardation is common in rubella which is associated with cardiac anomalies.
   - Large-for-date babies are born if the mother is diabetic. Such babies usually have associated cardiac defects. Infants with transposition of great arteries (TGA) also weigh more than expected

Neonatal and Postnatal History

Specific problems that arise during the neonatal and postnatal period should be enquired to arrive at a diagnosis. These are as follows:

- Neonatal cyanosis—bluish discolouration of the body on crying/feeding may be seen in congenital cyanotic heart diseases.
- Breathing difficulties (respiratory distress syndrome).
- Feeding problems—duration of feeding. Poor feeding is due to fatigue and dyspnoea in congestive cardiac failure (CCF).
- Arteriovenous malformations.
- Delay in growth is seen in congenital heart diseases such as TOF and VSD. Weight gain is poor and delayed in children with CCF of long duration and cyanosis. Weight is affected more than height.

Developmental History

Delayed development is seen in the following conditions:

- Down's syndrome is associated with endocardial cushion defects, conotruncal anomalies, VSD and ASD.
- William's syndrome is associated with supravalvular aortic stenosis (AS).

Nutritional History

Congestive cardiac failure is seen in kwashiorkor. Cardiomyopathy is seen in protein energy malnutrition.

Immunisation History

Ask if the child has been given all the routine immunisations. Also note if any optional immunisations are given.

History of Allergy and Contact

Tuberculosis infection is more common in cyanotic heart diseases such as TOF.

Family and Sibling History

- Consanguineous marriage

- Maternal age at conception: The elder the mother (older than 35 years) at the time of conception, more is the possibility of giving birth to a child with Down's syndrome and associated cardiac defects.
- Age of the father: The incidence of Marfan's syndrome is high if the paternal age at the time of conception is above 40 years. This is associated with aortic regurgitation (AR).
- Heart disease in family: The incidence of congenital heart diseases in the general population is about 1% or, more precisely, 8 of 1000 live births. The incidence of congenital heart defect is more when another member in the family is suffering from congenital heart defects. Sudden unexpected death in the family may be associated with cardiac disorders. If the mother suffers from congenital heart disease herself, the incidence of congenital heart disease increases by 3%–4% in the child. If the first child suffers from congenital heart diseases, the probability of the second child suffering from cardiac disorders is increased by 25%.
- Hereditary diseases: A number of hereditary disorders are associated with congenital heart defects. Pulmonary stenosis (PS) is common in Noonan's syndrome. Leopard syndrome is associated with PS and cardiomyopathy.
- Rheumatic fever: Incidence of rheumatic fever is more common in cases of close contact within the family.
- Diabetes mellitus: Infants of diabetic mothers are more prone to develop congenital heart defects such as asymmetrical hypertrophy of the interventricular septum.

Socioeconomic History

- House—pukka/thatched
- Area of living—living area per family member
- Ventilation
- Water supply
- Per capita income
- Hygiene
- Sanitation facilities available—unhygienic conditions and overcrowding predispose to rheumatic fever

This is followed by a detailed clinical examination, which will help to reach a diagnosis.

GENERAL EXAMINATION

The physical examination in every child should be individualised. However, the following points should be noted in a child who is suspected to have a cardiac disorder.

- General appearance—note whether the child is happy, anxious, cranky, fretful or sweating.
- Dysmorphic features/syndromes/chromosomal abnormalities—look for various syndromes such as Down's, Turner's, Cri-du-chat, Marfan's and William's syndrome as these are usually associated with congenital cardiac defects (Table 8.6). Also look for cardiac anomalies in any child who presents with multisystem malformations.

TABLE 8.6 Some Common Syndromes Associated with Cardiac Defects

Disorder/Syndrome	Common Cardiac Defects
Apert's syndrome	VSD, TOF
Crouzon's disease	PDA, COA
Ellis–van Creveld syndrome	Single atrium
Holt–Oram syndrome	ASD (ostium primum), VSD
Leopard syndrome	PS
Marfan's syndrome	AR and MR
William's syndrome (Elfin facies)	Supravalvular AS, peripheral pulmonary artery stenosis
Noonan's syndrome	PS
Kartagener's syndrome	Dextrocardia with situs inversus Transposition of great vessels
5p- (Cri-du-chat syndrome)	VSD, PDA, ASD
Trisomy 13 (Patau's syndrome)	VSD, PDA, dextrocardia
Trisomy 18 (Edward's syndrome)	VSD, PDA, PS
Trisomy 21(Down's syndrome)	Endocardial cushion defects, VSD
Turner's syndrome (XO)	COA, AS, ASD.
Klinefelter's variant (XXXXY)	PDA, ASD

AR—aortic regurgitation, AS—aortic stenosis, ASD—atrial septal defect, COA—coarctation of aorta, MR—mitral regurgitation, AS—aortic stenosis, PDA—patent ductus arteriosus, PS—pulmonary stenosis, TOF—tetralogy of Fallot, VSD—ventricular septal defect.

TABLE 8.7 External Markers of Congenital Cardiac Defects

External Markers	Syndrome/Disorder	Associated Cardiac Defects
Elfin facies	William's syndrome	Supravalvular aortic stenosis, pulmonary artery stenosis
Mongoloid facies, single palmar crease, hypotonia, mental retardation	Down's syndrome	Endocardial cushion defects, ventricular septal defect, patent ductus arteriosus
Hypertelorism, short philtrum, downslanting eyes, deficient cell-mediated immunity, hypocalcaemia	DiGeorge syndrome	Interrupted aortic arch, truncus arteriosus, ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot
Chondrodystrophic dwarfism, polydactyly, short distal limbs, neonatal teeth, bell-shaped chest	Ellis–van Crevald syndrome	Atrial septal defect
Webbed neck, cubitus valgus, short stature	Turner's syndrome	Coarctation of aorta
	Noonan's syndrome	Pulmonary stenosis
Absent radii, normal thumb, thrombocytopenia	TAR syndrome (thrombocytopenia—absent radius syndrome)	Atrial septal defect
Arachnodactyly, subluxation of lens, tall stature	Marfan's syndrome	Aortic aneurysm, aortic regurgitation/mitral regurgitation

- External markers of cardiovascular disorders—external markers or clinical findings which are associated with congenital cardiac anomalies are given in Table 8.7.
- Nutritional status—well-nourished or undernourished. Child usually presents with failure to thrive in long-standing cardiac failure and cyanotic heart diseases. Obesity is associated with hypertension and coronary artery disease.
- Level of consciousness.
- Decubitus—child is comfortable in sitting posture due to orthopnoea in cardiac failure.
- Pallor—due to anaemia or vasoconstriction (congestive heart failure [CHF], shock).
- Cyanosis—central cyanosis due to decreased oxygenation is seen in the tongue, nail beds and conjunctiva. It may be seen at rest/exercise/crying. Peripheral cyanosis is seen in the extremities due to sluggish blood flow in CHF and after cold exposure.
- Plethora due to polycythaemia is seen in cyanotic heart diseases. Polycythaemic infants may appear cyanotic even with normal arterial saturation.
- Jaundice may be seen in cardiac cirrhosis. Exaggerated physiological jaundice may be seen in newborns with severe CHF and congenital hypothyroidism. Patent ductus arteriosus and PS are common in infants with congenital hypothyroidism.
- Respiratory rate and effort—dyspnoea and tachypnoea are seen in children with heart failure. Also look for use of accessory muscles of respiration. A resting respiratory rate of more than 60 breaths/minute is abnormal at all ages.
- Clubbing is seen in infective endocarditis and cyanotic heart diseases.
- Oedema (pedal/sacral) is seen in CCF and restrictive heart diseases or severe tricuspid valve disease.
- Sweating on forehead is seen in infants with CCF.
- Chest and spine deformity—kyphosis and scoliosis lead to shifting of the apical impulse. Also look for scars of surgery and straight back.
- Skin—rheumatic nodules over the extensor aspect of the body (rheumatic fever).
- Dental caries predispose to infective endocarditis in a child with cardiac defects.
- Features of rheumatic fever—fever, subcutaneous nodules, chorea, swelling of joints and erythema marginatum.
- Markers of infective endocarditis—petechiae, splinter haemorrhage, Roth's spot, Osler's node and Janeway lesion.

Anthropometry

- Weight—failure to gain weight occurs in the

presence of chronic heart failure or cyanotic heart diseases. The weight may be increased in the presence of acute heart failure due to oedema.

- Height—Marfan's syndrome is associated with tall stature. Short stature is seen in Turner's syndrome (Table 8.7).
- Head circumference—microcephaly is seen in Down's syndrome.

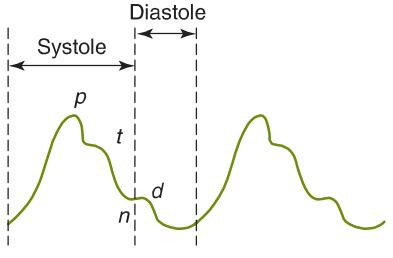
Arterial Pulses

Any abnormalities in the cardiac function or the arterial system are reflected in the pulse. Pulse should be palpated in carotid, brachial, radial, femoral, popliteal, posterior tibial and dorsalis pedis arteries and assessed for rate, rhythm, character, volume, radiofemoral delay and condition of vessel wall (Fig. 8.1).

Feel the radial pulse with the tip of the fingers. Feel the carotid artery with the thumb; right carotid artery with the examiner's left thumb and the left carotid with the right thumb. Press the thumb backwards at the medial border of sternomastoid muscle at the level of thyroid cartilage.

Always compare the pulses with the other side. Do not palpate both the carotids simultaneously. It may lead to impairment of blood flow to the brain and thereby lead to syncope.

1. *Rate*—normal pulse rate varies with age and condition of the patient. For normal pulse rates at various ages, see Chapter 3, section *Pulse*, page 78. Pulse rate is increased (tachycardia) in fever, CHF and arrhythmias (sinus tachycardia). It is decreased (bradycardia) in athletes, complete heart block, hypothyroidism and drug intake (β-blockers, digoxin). Count the rate by palpating the radial artery. Holding the hand and counting the rate may cause anxiety in the patients. So try to divert the attention by asking other questions such as what are you studying? Who is your close friend? etc. Count for at least 30 seconds. *Pulse deficit* is the difference between the heart rate and the pulse rate. Both should be simultaneously counted for one full minute. Count by auscultating over the precordium for heart rate and palpating at the radial artery for pulse rate. In atrial fibrillation, the pulse rate will be less than the heart rate.
2. *Rhythm*
   - Regular
   - Irregular—regularly irregular or irregularly irregular as in atrial fibrillation. Sinus arrhythmia (variation with inspiration) is normal
3. *Volume* is best assessed in the carotids.
   - Normal volume pulse is seen in normal children, ASD and TOF.
   - Large volume pulse (bounding pulse) is seen in PDA, AR, persistent truncus arteriosus, anaemia, high fever and arteriovenous fistula.
   - Small volume pulse (weak, thready pulse) is seen in heart failure, shock or in leg of a patient with coarctation of aorta. Arterial injury due to previous cardiac catheterisation may result in small volume pulse in the affected limb.
4. *Character* is determined by both the stroke volume and the arterial resistance. This is best studied at the carotids (Fig. 8.2). Look for the following characters:
   - *Water-hammer pulse (Corrigan's pulse, collapsing pulse)* is a large volume collapsing pulse. It has a rapid upstroke and rapid downstroke with ill-sustained crest. It is better felt in the radial artery with the arm elevated above the heart level. It is seen in AR, arteriovenous fistula and PDA.



Normal pulse

p—percussion wave, *t*—tidal wave, *d*—dicrotic wave, *n*—dicrotic notch

FIGURE 8.1 Normal arterial pulse.

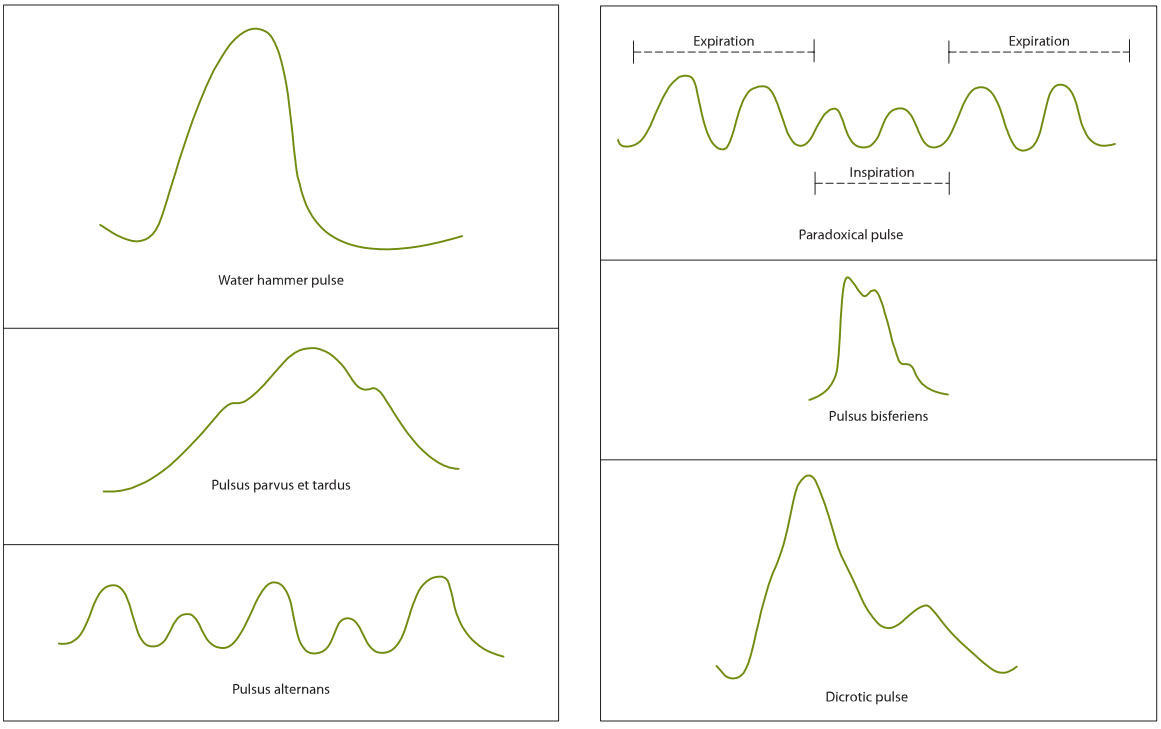


FIGURE 8.2 Abnormal pulses.

- *Pulsus parvus et tardus (pulsus tardus et parvus, slow rising pulse)* is seen in AS. This pulse is of small volume (parvus) with a slow rising character and a late systolic peak (tardus) due to left ventricle outflow obstruction. Earlier it was known as anacrotic pulse. It is also known as plateau pulse.
- *Pulsus alternans* is seen in left ventricular failure. Due to the left ventricular failure, the blood from the left ventricle is not emptied completely. This leads to increased diastolic volume for the next stroke. According to Starling's law, the force of contraction is directly proportional to the length of the muscle fibre. Hence, the heart will contract with more force and will cause an increased pulse volume in the next beat. As the heart is effectively emptied, the length of muscle fibre will decrease which leads to decreased force of contraction. This cycle alternates with each other, hence alternating strong and weak pulse will be felt. This is called pulsus alternans.
- *Pulsus paradoxus* is a misnomer. It occurs due to an exaggerated physiological fall in systolic blood pressure during inspiration. Normally, during inspiration, the fall in the intrathoracic pressure leads to decreased inflow of blood into the left atrium. This leads to fall in systolic blood pressure. In pulsus paradoxus the fall in the systolic pressure is more than 10 mm Hg (Fig. 8.3). This occurs in pericardial effusion, constrictive pericarditis, acute severe asthma and superior vena cava (SVC) obstruction. This sign is better detected by blood pressure measurement.
- *Reverse pulsus paradoxus* refers to a rise in systolic blood pressure during inspiration. It occurs in idiopathic hypertrophic subaortic stenosis, atrioventricular dissociation and in patients of left ventricular failure on positive pressure ventilation.

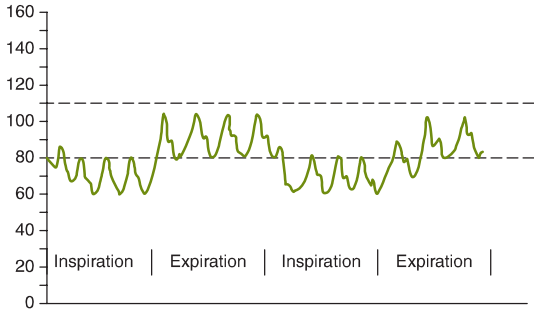


FIGURE 8.3 Pulsus paradoxus.

- *Jerky pulse*—in hypertrophic obstructive cardiomyopathy (HOCM), the pulse is of normal volume, rapidly rising and ill-sustained.
- *Pulsus bigeminus* consists of alternating strong and weak beats followed by a pause. It occurs due to premature ventricular contraction (or ventricular ectopic beat) that follows each regular beat. (In pulsus alternans, alternate beats of the failing left ventricle generate lower systolic pressure. This is usually recognised only during the measurement of blood pressure. When the cuff of the sphygmomanometer is maintained at a higher pressure, only the stronger alternate beats are heard. The compensatory pause is absent in pulsus alternans.)
- *Pulsus bisferiens* (biphasic pulse, bisferiens pulse) refers to twice beating pulse in systole (bisferious means striking twice) and occurs in mild AS with severe AR, isolated but severe AR and HOCM.
- *Pulsus dicroticus*—only one contraction of the ventricles is present for every two beats of the pulse. Note that in pulsus bigeminus, there are two contractions of the heart which follow each other rapidly and are separated from the preceding and succeeding contractions by a long pause.

5. *Condition of the vessel wall*—assess the vessel wall thickness. Walls will be thickened in atherosclerosis which is common in adults.
6. *Whether felt in all palpable peripheral vessels*—weak lower limb pulses are seen in coarctation of aorta.
7. *Radio femoral delay*—femoral pulse is felt after the radial pulse in coarctation of aorta (which is usually postductal).
8. *Radio-radial delay*—it occurs when the coarctation of aorta is preductal (proximal to or involving the subclavian artery) and in subclavian artery stenosis due to aneurysm. The right radial pulse is felt earlier than the left radial pulse.

Vital Signs

Blood Pressure

Normal blood pressure (BP) in children varies with age (see Chapter 3, section *Normal Blood Pressure in Children*, page 80). Approximate blood pressure can be calculated in children by using the following formulae:

Systolic pressure = Age (years) × 2 + 90
Diastolic pressure = Age (years) + 60

Methods used to measure the blood pressure in children:

- Auscultatory method (sphygmomanometer)
- Palpatory method
- Flush method
- Oscillometry method
- Doppler method

Precautions to be taken while measuring the BP using a sphygmomanometer are as follows:

- Cuff should cover at least two-thirds of the upper arm.
- Blood pressure apparatus should be at the level of the upper arm.
- Lower end of the cuff should end 2–3 cm above the cubital fossa.
- Bladder of the sphygmomanometer cuff should completely encircle the arm.
- Patient should not be anxious (this will result in high BP reading).
- The size of sphygmomanometer cuff used will vary with the age (Table 8.8). A sphygmomanometer cuff which is too narrow will result in high BP reading, and a cuff which is too wide will produce a lower reading. Use of narrow cuff results in poor compression of the artery, hence a high pressure is required to induce the vascular

TABLE 8.8 Various Cuff Sizes Used for Various Age Groups

Age	Cuff Sizes (cm)
Newborn	2.5
<2 years	5
3–4 years	7.5
5–9 years	10
10–14 years	12.5

sounds. If the cuff is too wide, the lower segment of the compressed artery causes greater decrement in flow because of increased resistance and there is a tendency for the pulse to disappear before it reaches the lower edge of the cuff. This causes a low recording of the BP. The cuff selection is important in children because of the wide variation of body dimensions in children.

Pulse pressure is the difference between the systolic and diastolic pressure (normal: 30–60 mm Hg).

Mean arterial pressure is the product of the cardiac output and total peripheral resistance (normal: 100 mm Hg).

$$\text{Mean arterial pressure} = \text{Diastolic pressure} + \text{1/3 of pulse pressure}$$

Heart Rate. This is increased in presence of heart failure. Normal heart rate at various ages is given as follows:

<6 months: 120–160/minute
6–12 months: 110–120/minute
1–5 years: 95–110/minute
6–12 years: 80–110/minute
>12 years: 60–100/minute

Respiratory Rate

It is increased in cardiac failure.

Temperature

It is raised in infective endocarditis. Hypothermia is seen in cardiogenic failure or shock.

CARDIOVASCULAR EXAMINATION

Inspection

- Shape and symmetry of the chest wall
- Chest deformities such as pectus excavatum
- Precordial bulge
- Engorged veins over the chest wall
- Tracheal position
- Apical impulse
- Visible pulsations (aortic area, pulmonary area, epigastric, suprasternal, carotid areas and the back)
- Neck veins—engorged or not

Jugular Venous Pressure

Jugular venous pressure is an indirect measure of central venous pressure and reflects the pressure in the right atrium. This is because the internal jugular vein has no valves, runs a fixed course, does not go through the muscle plane and is in direct communication with the right atrium.

Technique of Measurement. Keep the patient at 45° with the head and neck adequately supported. Turn the head to left side. Focus a beam of light tangentially over the vein. The upper level of pulsations in the internal jugular vein is seen. In normal children, the pulsations lie behind the sternum and cannot be seen. If the JVP is raised, the pulsations are seen in the neck. The vertical distance between the sternal angle (taken as zero point) and the upper border of the oscillating column is measured. This is done by drawing a transverse line over the upper border of the oscillating column. Another horizontal line is drawn at the level of sternal angle. The vertical distance between both the horizontal lines measures the venous pressure. (Sternal angle is a fixed bony landmark that corresponds to midatrium irrespective of the position of the child.) It is said to be elevated if the distance is more than 3 cm (Fig. 8.4).

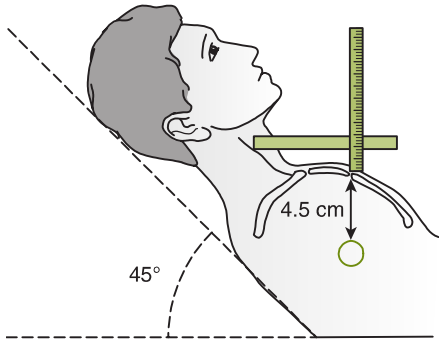
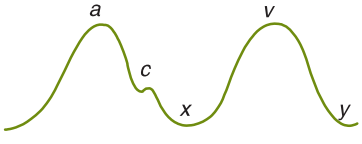


FIGURE 8.4 Measurement of JVP.

Jugular Venous Pressure Waveforms. JVP consists of the following waveforms (Fig. 8.5):

1. '*a*' *wave* corresponds to the right atrial contraction.
   - Absent in atrial fibrillation (atrial fibrillation—*a* wave is absent, *x* is decreased and *v* and *y* are seen).
   - Large *a* wave is seen in conditions where the right atrial contraction is stronger as in tricuspid stenosis, right ventricular hypertrophy (RVH) (pulmonary hypertension) and PS.
   - Cannon *a* wave is a giant *a* wave and occurs in cases with atrioventricular dissociation, where the atria contracts against a closed tricuspid valve, independent of the ventricular contraction. It is seen in complete heart block and ventricular tachycardia with atrioventricular dissociation.
2. '*c*' *wave* corresponds to closure of the atrioventricular valves and bulging of the tricuspid valve into the right atrium during ventricular systole.
3. '*v*' *wave* corresponds to the passive atrial filling with the tricuspid valve closed. It occurs in late systole. Large *v* waves are seen in tricuspid regurgitation. They are called *cv* or *v* waves (combination of *v* wave and loss of *x* descent).
4. '*x*' *descent* is due to right atrial relaxation and descent of tricuspid valve in the systole.
5. '*y*' *descent* is due to passive filling of the right ventricle at the start of diastole. Decreased *y* descent is due to obstruction to right ventricular filling.



a—atrial contraction
c—closure of A V valve
x descent—right atrial relaxation
v—atrial filling
y descent—opening of tricuspid valve with atrial emptying

FIGURE 8.5 Normal JVP.

Causes of Raised JVP. The JVP is grossly elevated and fixed in SVC obstruction. Other causes of the raised JVP include

- right ventricular failure,
- tricuspid stenosis or regurgitation,
- pericardial effusion and
- fluid overload.

Abnormalities of JVP are summarised in Table 8.9.

Hepatojugular Reflex. Press the right hypochondrial area for 30 seconds so that the liver is compressed. Normally, this causes rise in the JVP by less than 3 cm. This is followed by a gradual fall which occurs even if the pressure is sustained. Hepatojugular reflex is said to be elevated if compression over the liver causes elevation of JVP >3 cm, and there is sustained rise in JVP for >15 seconds. Hepatojugular reflex is elevated in the following conditions:

- Right heart failure
- Tricuspid regurgitation

It is absent in Budd–Chiari syndrome.

Kussmaul's Sign. Normally, the JVP falls during inspiration due to a fall in the intrathoracic pressure. Paradoxical rise with inspiration is known as Kussmaul's sign. It indicates impaired filling of the right ventricle. It can occur in the following conditions:

- Constrictive pericarditis
- Cardiac tamponade
- Right heart failure
- Restrictive cardiomyopathy

Differentiating Features of JVP from Carotid Pulsations. The jugular vein pulsations can be differentiated from carotid pulsations on the basis of the following features (Table 8.10):

- Better seen than palpable
- Occludable
- Characterised by a double waveform
- Varies with respiration
- Varies with sitting or standing posture

Visible Pulsations

Apart from the precordial and neck pulsations, also look for the pulsations in the suprasternal notch, epigastric region and back.

TABLE 8.9 Abnormalities of Jugular Venous Pressure

Jugular Venous Pressure	Mechanism		Conditions
Large *a* wave	Obstruction to tricuspid valve		Tricuspid stenosis Right atrial myxoma
	Non-compliant right ventricle		Pulmonary outflow obstruction Pulmonary hypertension Pulmonary stenosis
Cannon *a* wave	Right atrium closes against closed AV valve (A-V dissociation)		Complete heart block Ventricular tachycardia
Abnormal *x* descent	Decreased *x* descent		Tricuspid regurgitation
	Increased *x* descent		Atrial septal defect Pulmonary regurgitation Anomalous pulmonary venous connection
Large *v* wave	Excess filling of right atrium	From above	Atrial septal defect Total anomalous pulmonary venous connection
		From below	Tricuspid regurgitation
	Right atrial compliance is poor	From outside	Constrictive pericarditis
		From inside	Right atrial myxoma
Abnormal *y* descent	Decreased *y* descent		Tricuspid stenosis Right atrial myxoma
	Increased *y* descent		Tricuspid regurgitation Right ventricular failure Constrictive pericarditis

TABLE 8.10 Differentiating Features between Jugular and Carotid Pulsations

Features	Arterial Pulse (Carotid)	Venous Pulse (Jugular)
Site	Seen internal to sternomastoid	In the triangle formed between the two heads of sternomastoid and the clavicle
Site in relation to sternomastoid	Medial to the muscle	Lateral to the muscle
Palpation	More felt than seen (palpable)	More seen than felt (not palpable)
Number of waves	Single	Multiple
Variation	Does not vary	Varies with • Posture changes • Respiration (falls in inspiration) • Pressure over the liver
Obliteration	Cannot be obliterated	Can be obliterated by pressure over the neck veins
Level	No upper level	Has a definite upper level which falls during inspiration
Wave pattern	Dominant outwards	Dominant inwards

Suprasternal Notch. The pulsation in this site is due to aortic lesions. It may be due to aneurysm of the arch of aorta or unfolding of the aorta. The aneurysm of the arch of aorta may be associated with a tracheal tug. Tracheal tug is pull of trachea into the thoracic cavity with every systole in cases with aortic aneurysm.

Epigastric Pulsations. Epigastric pulsations are commonly seen in the following conditions:

- Pulsations of the liver in CHF with tricuspid regurgitation
- Thin persons
- Abdominal aorta aneurysms
- Right ventricular hypertrophy
- Tricuspid stenosis

Examination of the Back. Pulsations at this site may be due to the collaterals in coarctation of the aorta. This is called Suzman's sign. The pulsation is prominent over the scapula and is best visualised with the patient bending forwards.

Palpation

Precordium is palpated to find any abnormalities and to confirm the findings of inspection. The following points should be noted:

1. Tracheal position should be confirmed by palpation. Presence of tracheal tug should be noted. It refers to the pull of trachea into the thoracic cavity with each systole and is seen in cases of aortic aneurysm
2. Apical impulse—the left ventricle and the left ventricular portion of the interventricular septum produce the apical impulse. It refers to the lowest and outermost point of definite cardiac impulse, which gives maximum thrust to the palpating finger. Apical impulse is examined for the following features:
   (a) Location is noted in terms of intercostal space (ICS), distance from the midclavicular line and relation to midclavicular line (medial/lateral). The normal site of the apical impulse varies with age (Table 8.11). The causes of shift of apical impulse are as follows:

TABLE 8.11 Normal Variation in Location of Apical Impulse with Age

Age	Position of Apical Impulse	Relation to Midclavicular Line
Infancy	In the left fourth intercostal space	Just lateral to the midclavicular line
Approximately 5 years	In the left fifth intercostal space	In the midclavicular line
Older children and adults	This is situated in the fifth intercostal space	Just medial to the midclavicular line

- Left ventricular hypertrophy (LVH)—apex will be shifted downwards and outwards
- Right ventricular hypertrophy—apex shifted outwards
- Dextrocardia
- Pseudodextrocardia
- Respiratory causes—collapse, pleural effusion, pneumothorax, fibrosis, etc.
- Diaphragmatic hernia
- Eventration of diaphragm
- Skeletal deformities—scoliosis, kyphosis

(b) Character—normal/abnormal. Abnormal characters of apical impulse are as follows:

- Tapping apical impulse—seen in MS.
- Heaving apical impulse—thrust over the palpating finger for more than two-thirds of the systole due to pressure overload (AS)
- Hyperdynamic apical impulse—felt over more than one space due to volume overload (mitral regurgitation [MR]). It occupies more than one-third and less than two-thirds of the systole (Table 8.12)

TABLE 8.12 Differentiating Features between Heaving and Hyperdynamic Apical Impulse

Features	Heaving Apical Impulse	Hyperdynamic Apical Impulse
Site	Normal	Shifted outwards and downwards
Duration	More than two-thirds of the systole Sustained thrust	Less than two-thirds of systole Diffuse, ill-sustained thrust
Site	Felt in one intercostal space	Felt in more than one intercostal space
Pathological changes	Concentric hypertrophy due to pressure overload	Dilatation of the ventricle due to volume overload
Causes	Aortic stenosis Hypertension Coarctation of aorta	Mitral regurgitation Aortic regurgitation Ventricular septal defect Patent ductus arteriosus

- Diffuse apical impulse—left ventricular aneurysm
- Double apical impulse—AS with AR, HOCM and left ventricular aneurysm
- Triple or quadruple apical impulse—HOCM.

(c) Apical impulse may not be visible in certain cases. The causes of absent apical impulse are

- Obese children
- Apical impulse behind the ribs
- Pericardial effusion
- Pleural effusion
- Pneumothorax
- Hydropneumothorax
- Emphysema

3. Thrills—these are palpable vibrations of murmurs which accompany any organic murmur of grade III or more. Note the location and timing (systolic/diastolic) of thrills (Table 8.13).
4. Parasternal heave—a palpable thrust, which lifts the palpating hand, is felt in cases with RVH and left atrial enlargement. It is palpated by the ulnar aspect of the palm. This can also be demonstrated by placing a pen on the left parasternal region, which will move perpendicular to the chest wall. Grading of parasternal heave is given in Table 8.14.
5. Palpable sounds
   - First heart sound in MS
   - Second heart sound in cases with pulmonary hypertension
   - Pericardial rub in cases with pericarditis.
6. If dilated veins are present, find the direction of flow in the dilated veins. The flow will be downwards when the SVC is blocked. The flow will be from below upwards when the inferior vena cava (IVC) is obstructed.

TABLE 8.13 Conditions in Which Murmurs Are Palpable as Thrills

Location	Conditions
Carotid thrill	Felt over the carotids in aortic stenosis
Aortic area	
First aortic area	A systolic thrill is palpable in aortic stenosis
Second aortic area	Early diastolic thrill is palpable in aortic regurgitation
Pulmonary area	Pulmonary stenosis
Left lower parasternal area	Systolic thrill is palpable in ventricular septal defect
Second left intercostal space	Continuous thrill—rupture of sinus of Valsalva, patent ductus arteriosus
Apical area	Systolic thrill is palpable in mitral regurgitation and diastolic thrill in mitral stenosis

TABLE 8.14 Grading of Parasternal Heave

Grades	Examination Findings
I	Instant lift only visible not palpable
II	Visible and palpable; the lift can be obliterated
III	Visible and palpable; the lift can not be obliterated

Percussion

The left border corresponds to apex. The right border corresponds to right sternal margin. Percussion of the heart is done to see the enlargement of the dullness of the cardiac region. The percussion of the pericardium is useful in the following conditions:

1. Cardiac causes—cardiomegaly, pericardial effusion, pulmonary artery dilatation, dilated cardiomyopathy, etc. See if the dullness extends beyond the apical impulse as in case of pericardial effusion.
2. Respiratory causes—in finding the cause of displaced heart due to lung conditions such as pleural effusion, hydropnemothorax, collapse and fibrosis.
3. Presence of a diaphragmatic hernia and eventration of diaphragm can be suspected.

Auscultation

Auscultation is done for heart sounds, murmurs and added sounds such as pericardial rub. Auscultatory areas in the precordium (Fig. 8.6) are as follows:

1. Mitral area—fifth left ICS in the midclavicular line (corresponds to the apex beat).

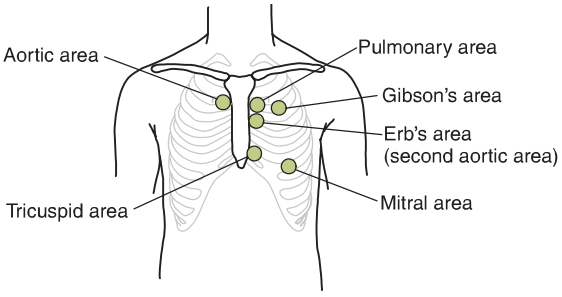


FIGURE 8.6 Auscultatory areas of the heart.

2. Tricuspid area—fourth left ICS just lateral to the lower end of the sternum.
3. Aortic area
   - First aortic area—second right ICS close to sternum
   - Second aortic area or Erb's area—third left ICS close to sternum; the early diastolic murmur (EDM) of AR and pansystolic murmur of VSD are best heard here.
4. Pulmonary area—second left ICS close to sternum.
5. Gibson's area—second left ICS away from sternum; the murmur of patent ductus arteriosus is best heard here.
6. Other areas of auscultation:
   - Carotids
   - Supraclavicular region
   - Infraclavicular region
   - Axillary region
   - Back—interscapular and infrascapular region, bruits in the back.

Auscultate these areas for the following sounds:

- Heart sounds (S_1, S_2, S_3 and S_4)
- Heart murmurs
- Gallops
- Opening snap (OS)
- Ejection clicks
- Pericardial knocks
- Pericardial rub
- Diastolic knock
- Prosthetic valve sounds

Heart Sounds

The heart sounds are audible vibrations of variable intensity, frequency and quality generated by beating of heart, closure of heart valves and the resultant blood flow through it.

First Heart Sound (S_1). It is produced by the closure of atrioventricular valves (mitral valve and tricuspid valves) and is best audible at the apex. S_1 indicates the beginning of the ventricular systole. The mitral and tricuspid valves do not close simultaneously. As the time interval between the closure of the two valves is less than 30 milliseconds, the split is not normally heard but can be appreciated in a phonocardiogram. The intensity of the first heart sound is influenced by the following factors:

- Position of the atrioventricular valve cusps at the onset of ventricular systole. Loud first sound is produced if the valve cusps are widely placed (as in high output states such as ASD, VSD and PDA) and muffled if they are close to each other.
- Heart rate—in tachycardia loud S_1 will be heard.
- Pliability of the valve cusps—the loud S_1 is heard only when the valve is pliable. When the valve is calcified, the pliability is lost and S_1 becomes muffled.

First heart sound may be of normal, soft, loud or variable intensity.

Soft S_1: It is seen in the following conditions:

- Mitral regurgitation
- Tricuspid regurgitation
- Ventricular dysfunction
- Calcified, stenosed mitral valve
- Calcified, stenosed tricuspid valve
- Aortic regurgitation
- Conditions associated with prolonged P-R interval (digitalis overdose)
- Miscellaneous conditions—emphysema, thick chest wall and obesity (the heart sounds will be muffled)

Loud S_1: It is seen in the following conditions:

- Mitral stenosis
- Tricuspid stenosis
- Atrial septal defect
- Mechanical prosthetic valve
- High output states (exercise, severe anaemia, thyrotoxicosis, fever, etc.)
- Short P-R interval, tachycardia

- Atrial myxoma
- In normal children

Varying intensity of S_1: It is seen in the following conditions:

- Atrial fibrillation
- Complete heart block
- Extrasystoles

Canon sound (*bruit de canon*): It is loud first heart sound heard intermittently in complete atrioventricular block (complete heart block) and in interference, dissociation when the ventricles contract shortly after the atria. This will be associated with short P-R interval.

Splitting of S_1: The components of first heart sounds are those due to mitral valve closure (M_1) and tricuspid valve closure (T_1). Normally, tricuspid component is delayed by about 20–30 milliseconds as compared to the mitral component. This is not appreciable on auscultation; hence, we perceive it as a single sound. This split can be appreciated in any condition which leads to early closure of the mitral valve or delayed closure of the tricuspid valve, so that the time interval between the two components is increased. The causes of split S_1 are as follows:

- Right bundle branch block (RBBB)
- Pulmonary hypertension
- Left ventricular pacing
- Ectopic beats
- Idioventricular rhythm of left ventricle

Reverse splitting of S_1: If the mitral component is delayed so that the tricuspid component is heard earlier than the mitral component, it leads to reverse splitting. The causes of reverse splitting of S_1 are as follows:

- Right ventricular pacing
- Ectopic beats
- Idioventricular rhythm of right ventricle

Second Heart Sound (S_2). It is produced by the closure of aortic and pulmonary valves and marks the beginning of diastole. The opening of the normal valves is inaudible. The closure of the aortic valve precedes the closure of the pulmonary valve. Hence, the aortic component is heard prior to the pulmonary component and leads to normal splitting of the second heart sound. This is normally appreciable during inspiration.

1. *Soft S_2:* It is seen in the calcified pulmonary/aortic stenosis.
2. *Loud S_2:* It is seen in the following conditions:

(a) Aortic component—systemic hypertension
(b) Pulmonary component
- Increased pulmonary blood flow—PDA, ASD and large VSD
- Pulmonary hypertension
- Pulmonary artery dilatation

(c) Summation of A_2 and P_2—any condition that leads to delayed closure of the aortic valve or early closure of pulmonary valve will lead to narrowing of split. When the time interval of the split is 30 milliseconds or less, the second sound will be heard, as a single sound and the intensity will be loud, due to the summation effect. It will be seen in the following conditions where A_2 and P_2 are narrowly split:
- Atrial stenosis
- Pulmonary hypertension
- Left bundle branch block (LBBB)

3. *Split second sound:*

(a) Normal split (Fig. 8.7a)
(b) Wide and variable splitting (Fig. 8.7b)
(c) Fixed and wide splitting—ASD, PS and RBBB (Fig. 8.7c)
(d) Reverse splitting—it is seen in LBBB and severe AS (Fig. 8.7d)
(e) Narrow splitting—leading to summation of A_2 and P_2 (Fig. 8.7e)

4. *Single S_2:* Only the pulmonary or aortic component may be heard due to absent A_2 or P_2, respectively (Fig. 8.7e).

(a) Absent A_2
- Atrial stenosis (severe)
- Aortic atresia

(b) Absent P_2
- Pulmonary stenosis (severe)
- Pulmonary atresia
- Transposition of great vessels
- Tetralogy of Fallot
- Truncus arteriosus (condition associated with single semilunar valve)

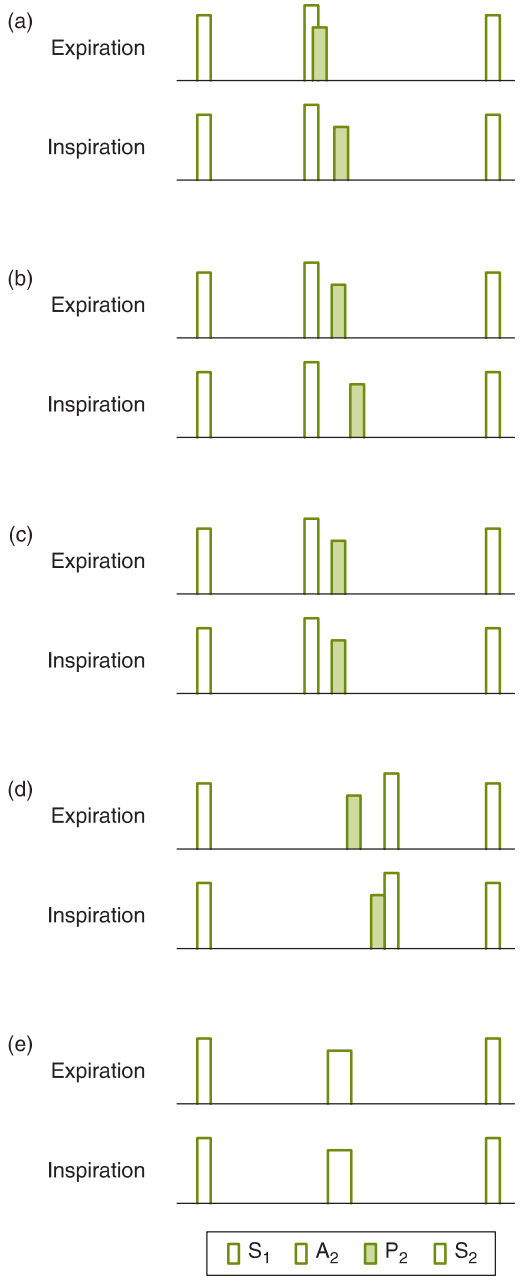


FIGURE 8.7 Second heart sound in pulmonary area. (a) Normal variation in the degree of splitting with respiration. (b) Wide and variable splitting. (c) Fixed and wide splitting. (d) Reverse splitting. (e) Single second sound—combination of A_2 and P_2 or either of these. Also note the relative intensities of A_2 and P_2.

Third Heart Sound (S_3). Protodiastolic sound/ventricular gallop is produced by initial passive filling of the ventricles. It may be confused with split second sound or OS. It is heard best with the bell of the stethoscope at the apex. It is normally present in children and athletes. The causes of pathological S_3 are as follows:

1. High output states
2. Congenital heart diseases
   - Atrial septal defect
   - Ventricular septal defect
   - Patent ductus arteriosus
3. Regurgitant lesions
   - Aortic regurgitation
   - Mitral regurgitation
   - Tricuspid regurgitation
4. Hypertrophic obstructive cardiomyopathy
5. Constrictive pericarditis
6. Systemic hypertension
7. Pulmonary hypertension
8. Ventricular failure

Fourth Heart Sound (S_4). Presystolic gallop/atrial gallop is produced by a rapid emptying of the atrium into a non-compliant ventricle. It may be confused with ejection click. It is always pathological and is heard in the following conditions:

- Hypertrophic obstructive cardiomyopathy
- Systemic hypertension
- Ventricular failure
- Pulmonary hypertension

Added Sounds

Gallop Rhythm. It refers to tripling or quadrupling of heart sounds. It resembles the canter of a horse.

1. *Triple rhythm:* When the third or the fourth heart sound is heard along with first and second heart sounds, it is called *triple rhythm*. It can be of the following types depending on where in the cardiac cycle the added sound comes:
   - Atrial gallop—where the first and second heart sounds are associated with atrial contraction: S_1, S_2 and S_4.
   - Ventricular gallop—where the first and

second heart sounds are associated with rapid ventricular filling: S_1, S_2 and S_3.

2. *Quadruple rhythm:* When all the four heart sounds are heard separately (Fig. 8.8a).
3. *Summation gallop* is seen in conditions associated with fast heart rate. S_3 and S_4 occur so close as to be indistinguishable and only three sounds are heard in one cardiac cycle.

Opening Snap. It occurs due to the opening of atrioventricular valves (Fig. 8.8b). It can be heard at the apex or at the left parasternal region. The causes of opening snap at the apex:

- Mitral stenosis
- Mitral regurgitation
- Ventricular septal defect
- Patent ductus arteriosus

Causes of opening snap at the left parasternal region:

- Tricuspid stenosis
- Tricuspid regurgitation
- Atrial septal defect

Ejection Click. It is a sharp, clicking sound arising from the cardiac valves due to sudden swelling of the pulmonary artery, abrupt dilatation of aorta or forceful opening of the aortic cusps. Depending on the timing of the click, it can be of the following types:

- Early systolic ejection click is seen in aortic and pulmonary valve stenosis (Fig. 8.8c).
- Midsystolic ejection click is seen in floppy mitral valve (Fig. 8.8b).

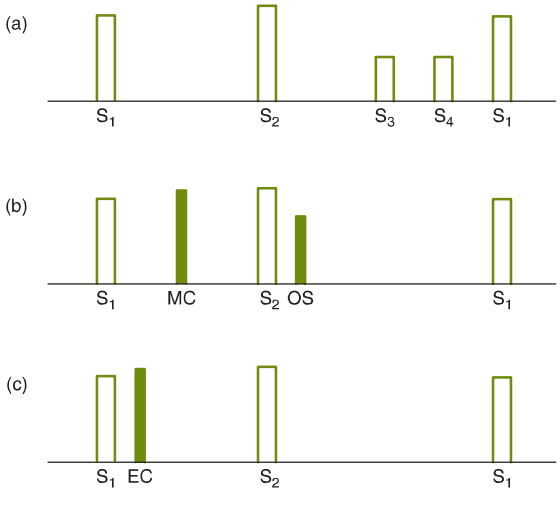


FIGURE 8.8 Relative positions of added sounds. (a) Quadruple rhythm. (b) Midsystolic click and diastolic opening snap. (c) Early ejection systolic click. *Abbreviations*: EC—ejection click, MC—midsystolic click, OS—opening snap.

Murmurs

Murmurs occur due to the turbulence caused by either an increased flow through a normal/stenosed valve or a normal flow through a stenosed valve/orifice. Auscultation should be done over the precordium, back and over the carotids. Note the various characteristics of murmur and the position of the patient in which the murmur is best heard. Some murmurs are changing murmurs, that is they change in intensity or character from time to time as in infective endocarditis, left atrial myxomas and atrial thrombosis.

Site. Note the site of maximal intensity of murmur. For instance, VSD murmur is best heard in the left third and fourth ICS in the parasternal region. Pulmonary ejection systolic murmur is best heard in the left second ICS (Table 8.15).

Timing. Timing of the murmur in relation to the ventricular activity (systolic, diastolic or continuous murmur) should be noted. Note whether the murmur extends throughout the systole or is confined to a shorter part of the cardiac cycle. The timing of the murmur is usually appreciated by palpating the carotid artery while auscultating the precordium. Note that only one carotid is palpated at a time. If both carotids are palpated simultaneously, the blood flow to the brain may be decreased leading to syncope or loss of consciousness.

1. *Systolic murmurs* are the murmurs heard during systole. They can be ejection systolic or regurgitant (usually pansystolic) depending on the timing of the murmur in relation to the ventricular systole (Table 8.16).

(a) *Regurgitant systolic murmurs* start immediately after the first heart sound and may continue to the second heart sound. They are usually pansystolic or holosystolic (Fig. 8.9a). The intensity of the pansystolic murmur is uniform

TABLE 8.15 Location of Murmur

Site	Murmur	Conditions
Mitral area	Middiastolic murmur Ejection systolic murmur	Mitral stenosis Aortic stenosis—conducted
Pulmonary area	Ejection systolic murmur	Pulmonary hypertension Atrial septal defect Tetralogy of Fallot Pulmonary stenosis
Aortic area—first	Ejection systolic murmur	Aortic stenosis
Aortic area—second	Early diastolic murmur	Aortic regurgitation
Tricuspid area	Pansystolic murmur	Tricuspid regurgitation
Second left intercostal space and left infraclavicular area	Continuous murmur	Patent ductus arteriosus
In the left third and fourth intercostal space in the parasternal region	Pansystolic murmur	Ventricular septal defect

TABLE 8.16 Type of Systolic Murmurs and Associated Cardiac Defects

Timing of Murmur	Differential Diagnosis
Regurgitant systolic murmurs	Ventricular septal defect Mitral regurgitation Tricuspid regurgitation
Ejection systolic murmur	
• Pulmonary area	Pulmonary stenosis Pulmonary hypertension Tetralogy of Fallot Atrial septal defect
• Aortic area	Aortic stenosis

throughout. Regurgitant systolic murmur may decrease and end before S_2 (not holosystolic) in some children with small VSD. Causes of pansystolic murmurs

- Ventricular septal defect
- Tricuspid regurgitation
- Mitral regurgitation

(b) *Ejection systolic murmurs (ESMs)* are due to the flow of blood in pulmonary or aortic outflow tracts. There is a gap between the first heart sound and murmur. The intensity murmur follows a diamond-shaped configuration with a midsystolic peak (Fig. 8.9b). The causes of ESMs are as follows:

- Pulmonary stenosis
- Aortic stenosis
- Pulmonary hypertension
- Tetralogy of Fallot

2. *Diastolic murmurs* are heard in the diastolic phase of the cardiac cycle. Three mechanisms by which they can be produced are semilunar valve regurgitation, atrioventricular (A-V) valve

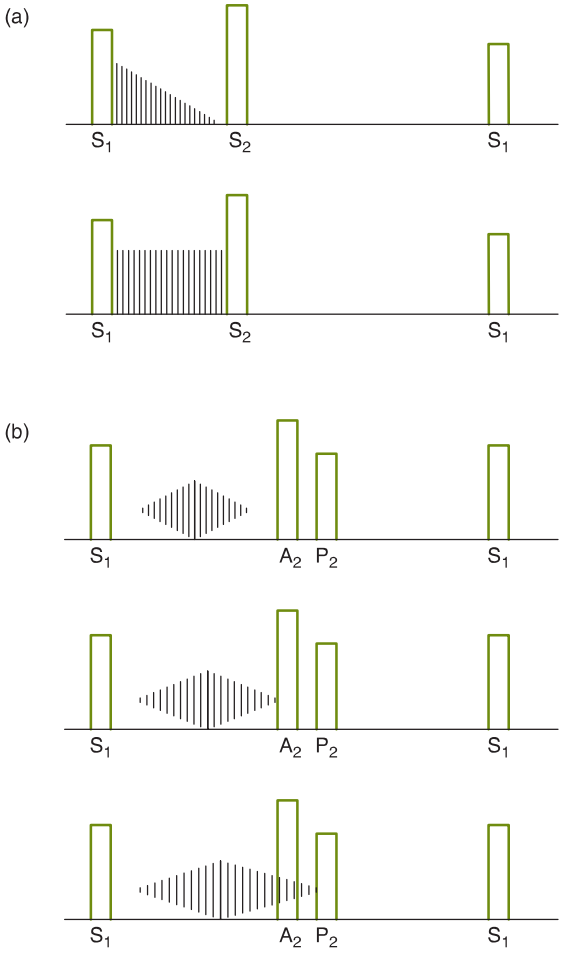


FIGURE 8.9 Types of systolic murmurs. (a) Regurgitant. (b) Ejection systolic.

TABLE 8.17 Timing of Diastolic Murmurs and Associated Cardiac Defects

Murmur	Conditions
Early diastolic murmur	Aortic regurgitation Pulmonary regurgitation (Graham Steell murmur—due to pulmonary regurgitation in pulmonary hypertension
Middiastolic murmur	Mitral stenosis Mitral regurgitation Tricuspid stenosis Tricuspid regurgitation Austin Flint murmur (AR) Atrial septal defect Ventricular septal defect Patent ductus arteriosus Total anomalous pulmonary venous drainage
Late diastolic or presystolic	Mitral stenosis Tricuspid stenosis

stenosis and increased blood flow through A-V valve (relative stenosis). According to the timing of murmur, they are classified as early diastolic, middiastolic and presystolic (or late diastolic) (Table 8.17, also see Fig. 8.10a)

(a) *Early diastolic (or protodiastolic) murmur* is decrescendo murmur which starts immediately after the second heart sound. The causes are as follows:

- Aortic regurgitation
- Pulmonary regurgitation

(b) *Middiastolic murmur (MDM)* starts after the second heart sound. There is a clear gap between the second sound and the murmur. It occurs due to functional or anatomic stenosis across the A-V valves. The causes across mitral valve are as follows:

- Mitral stenosis
- Left atrial myxoma
- Cor triatriatum
- Austin Flint murmur (AR)
- Ventricular septal defect
- Mitral regurgitation
- Patent ductus arteriosus

The causes across tricuspid valve are

- Tricuspid stenosis

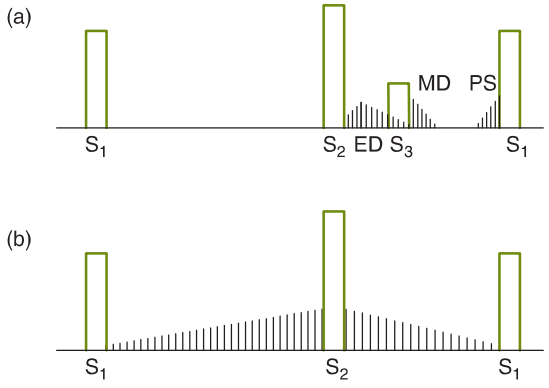


FIGURE 8.10 (a) Types of diastolic murmur. (b) Continuous murmur. *Abbreviations*: ED, early diastolic; MD, middiastolic; PS, presystolic or late diastolic.

- Tricuspid regurgitation
- Atrial septal defect
- Total anomalous pulmonary venous drainage (TAPVD)

(c) *Presystolic murmur* occurs in mitral and tricuspid stenosis.

3. *Continuous murmurs* start in systole and continue into diastole (Fig. 8.10b). The causes of continuous murmur are as follows:

- Patent ductus arteriosus
- Venous hum
- Aortopulmonary window
- Rupture of sinus of Valsalva
- Bronchopulmonary collaterals
- Arteriovenous shunt
- Pulmonary A-V fistula
- Coronary A-V fistula
- Peripheral pulmonary stenosis
- Anomalous left coronary artery
- After Blalock–Taussig shunt
- Mammary soufflé (seen in adults)
- VSD with AR
- MR with AR
- AS with AR

The last three conditions occur due to combination of a systolic and diastolic murmur and are known as to-and-fro murmur.

Intensity. The murmurs are graded according to the intensity of the murmur (Table 8.18). Also note whether the intensity is the same throughout or

TABLE 8.18 Grading of Murmurs

Grading	Character
Grade I	Very soft (heard in a quiet room)
Grade II	Soft, but easily audible
Grade III	Moderate—no thrill
Grade IV	Loud with thrill present
Grade V	Very loud with thrill, murmur heard with the stethoscope placed barely on the chest wall
Grade VI	Loud and audible with a stethoscope just off the chest wall

increasing or decreasing during systole and diastole. A crescendo murmur increases in intensity (e.g., MS, PDA), while a decrescendo murmur decreases in intensity (e.g., AR). Venous hum has no such changes.

Pitch. (High pitched/low pitched) See if the murmur is best heard with the bell or diaphragm of the stethoscope. A high-pitched murmur is best heard with the diaphragm of the stethoscope. Low-pitched murmurs are best heard with the bell of the stethoscope.

Character or Quality. The murmur may be soft, harsh, blowing, rough, vibratory or humming in quality. The murmurs may be rough when there is an obstruction to the blood flow as in cases with stenosed valves (AS, PS). The murmurs may be blowing in cases with incompetent valves (MR).

Conduction/Transmission. If the intensity of the murmur is same at two different areas, the murmur is said to be conducted. If the intensity decreases at two different areas, the murmur is said to be transmitted from the area of high intensity to the area of low intensity. Conduction in a specific direction means the intensity is the same in that direction, but decreases in all other directions.

Conducted murmur	Transmitted murmur
Same intensity	Decreased intensity
Same duration	Decreased duration

The murmurs originating from the pulmonary and tricuspid valves are usually well localised, while those of aortic and mitral valves may be conducted to other parts of the precordium. The functional or flow murmurs are usually heard over a wide area of the precordium. The ESM of the AS is loudest in the aortic area and will be radiated to the axilla and the apex.

The pansystolic murmur of MR is best heard in the mitral area and may be conducted to axilla or to the back.

Variation of the Murmur with Various Manoeuvres.

1. *Respiration:* During inspiration there is an increased flow to the right side of the heart due to negative intrathoracic pressure. At the same time, the flow to the left side of the heart will be decreased. The converse of this occurs in expiration. This leads to an accentuation of the right-sided murmurs during inspiration and that of the left-sided murmurs during expiration.
2. *Change in posture*: The venous hum murmur varies with posture.
3. *Certain manoeuvres (such as Valsalva):* In the Valsalva manoeuvre the patient is asked to take a deep breath and hold the breath against the closed mouth and nose. This causes an increase in the intrathoracic pressure, which will decrease the blood flow to the right side of the heart and increase the blood flow to the left side of the heart.

This is explained in detail in the section *Dynamic Auscultation,* page 306.

Description of Murmurs. A murmur should always be described under various headings as explained above, otherwise the description is incomplete and it may not be possible to reach at diagnosis clinically. Table 8.19 shows area-wise description of classical murmurs in some common heart defects.

Innocent Murmurs. These are also known as functional or benign murmurs (Fig. 8.11). They occur in the absence of anatomic or physiological abnormalities of the heart and circulation. These are accentuated during periods of febrile illness or other high-output states. Differentiating features from organic murmurs are given in Table 8.20.

Characteristic features are

TABLE 8.19 Description of Various Murmurs

Condition	Murmur	Description
Mitral area		
Mitral stenosis	Middiastolic murmur	Rough, rumbling, low-pitched murmur of grade __ best heard with the bell of the stethoscope with patient lying in left lateral position with breath held in expiration
Mitral regurgitation	Pansystolic murmur	High pitched, soft blowing pansystolic murmur of grade __ best heard with the diaphragm of the stethoscope, conducted/transmitted to axilla and back with patient lying in left lateral position with breath held in expiration
Tricuspid area		
Ventricular septal defect	Pansystolic murmur	High pitched, soft blowing pansystolic murmur of grade IV best heard with the diaphragm of the stethoscope in the left third and fourth intercostal space in the parasternal region
Aortic area		
Aortic stenosis	Ejection systolic murmur	Crescendo–decrescendo ejection systolic murmur of grade __ best heard with the diaphragm of the stethoscope conducted to carotids with the patient leaning forwards with breath held in expiration
Aortic regurgitation	Early diastolic murmur	High pitched, soft blowing, decrescendo early diastolic murmur of grade __ best heard with the diaphragm of the stethoscope in the second aortic area with the patient leaning forwards with breath held in expiration
Left second ICS		
Patent ductus arteriosus	Continuous murmur	Grade IV continuous murmur best heard with the diaphragm of the stethoscope in the left second intercostal space

TABLE 8.20 Differences between Innocent and Organic Murmurs

Features	Innocent	Organic
Thrill	Not associated with thrill	Associated with thrill
Site	Localised	Diffuse
Timing	Usually systolic	Systolic or diastolic
Quality	Usually soft, short	Rough or blowing in character
Structural defect	No evidence of valvular lesion	Evidence of valvular lesion
Age	Usually present in children	Any age

- Asymptomatic
- Normal cardiac silhouette on chest X-ray
- Normal electrocardiogram (ECG)
- Usually systolic, may be continuous
- Less than grade 3/6 with no radiation or transmission
- No cyanosis
- Normal pulses
- Normal heart sounds

Common innocent heart murmurs are as follows:

1. *Still's murmur:* It was described by George Still in 1909. It is characteristically described as a low-pitched vibratory or musical murmur heard in midsystole. It has a soft quality, is short in duration and is best heard between the left lower sternal border and the apex. There is no radiation of the murmur. It has a grade 2–3/6 in intensity. It is more common after 3 years of age and rare in infancy. No cardiac abnormalities are present. Examination is completely normal with normal blood pressure, heart sounds, X-ray, ECG and echocardiographic (ECHO) findings.
2. *Venous hum:* A continuous murmur is heard in the neck and the upper chest due to partial obstruction of the large veins (jugular venous system) of the neck. This may be due to kinking of vein at the transverse process of atlas. As the kinking of the vessels will lead to the venous hum, change in the position of the neck will relieve the obstruction due to the kinking and the hum can be obliterated. Venous hum has a louder diastolic component. It is best heard

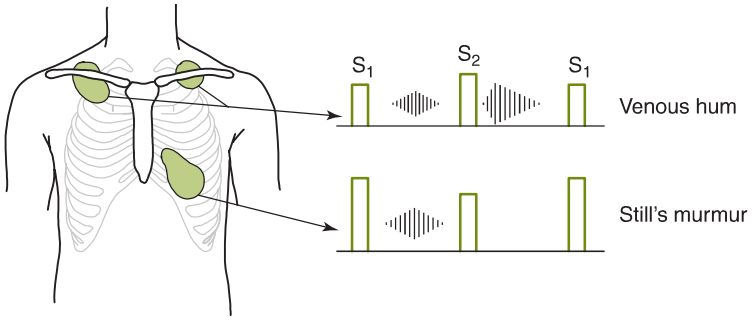


FIGURE 8.11 Innocent heart murmurs in children.

with the bell of the stethoscope in the right supraclavicular region with the head turned to opposite side in sitting posture. It disappears on lying down. The bell of the stethoscope is placed over the internal jugular vein just lateral to the sternocleidomastoid muscle.

Dynamic Auscultation

The murmurs originating from the heart vary with body positions or various interventions. During conventional auscultation, the patient remains static whereas the patient is asked to change position or perform certain activities during dynamic auscultation. This enables the physician to hear the murmurs and heart sounds better than in static conditions. These interventions are helpful in differentiating conditions with similar murmurs. Manoeuvres of dynamic auscultation include the following:

- Inspiration
- Expiration
- Valsalva manoeuvre
- Muller manoeuvre
- Squatting to standing
- Standing to squatting
- Passive leg exercise
- Isometric hand grip
- Transient arterial occlusion
- Administration of amyl nitrite
- Leaning forwards
- Chin turned upwards

Note if the murmur intensity increases, decreases or remains same after these manoeuvres. Some of these manoeuvres are discussed below.

Valsalva Manoeuvre

This is an attempted forced expiration in closed glottis when both the mouth and the nose are closed. Valsalva manoeuvre increases the intrathoracic pressure and thus obstructs the venous return in the right atrium. Its significance is as follows:

- Murmur of mitral valve prolapse becomes longer and louder during this manoeuvre. Mitral valve prolapse click moves more closer to S1 due to more redundancy of chordae tendinae.
- Hypertrophic obstructive cardiac myopathy (HOCM)—systolic murmur becomes louder during Valsalva manoeuvre. During this manoeuvre the thoracic pressure increases and the input to the right side of the heart is decreased. Thus, the ventricular diastolic volume is decreased. This decreased volume causes an increase in the obstruction to the outflow in HOCM causing an increase in the murmur.
- Valsalva manoeuvre makes the abdominal wall veins prominent.
- Valsalva manoeuvre increases the heart rate, increases the BP and then decreases the heart rate in that order. This sequence will be absent in autonomic neuropathy and CCF.
- Valsalva manoeuvre does not cause any change in the classical findings in ASD such as ESM and wide fixed split.
- Ejection systolic murmur in PS will be increased and that of AS will be decreased by Valsalva manoeuvre.
- Interval between OS and A_2 in MS will increase due to decrease in left atrial pressure. The intensity of MDM will decrease due to decreased

pressure gradient between left atrium and left ventricle.

Muller's Manoeuvre

It is the opposite of Valsalva manoeuvre. During this manoeuvre, a forced inspiration is attempted against a closed glottis with both mouth and nose closed. This manoeuvre decreases the intrathoracic pressure. Thereby it increases the flow to the right side of the heart and decreases the flow to the left side of the heart. Its significance is as follows:

- The murmurs originating on the right side will increase whereas the murmurs originating on the left side will become soft.
- Murmur of MVP decreases during this manoeuvre.

These manoeuvres of dynamic auscultation cause some physiological changes in the body and also have an effect on auscultation findings. These are summarised in Table 8.21. Right-sided murmurs are heard better during inspiration and left-sided murmurs are heard better during expiration. Dynamic auscultation in some common cardiac conditions is given in Table 8.22.

CLASSIFICATION

The cardiovascular disorders can be classified as congenital or acquired (Fig. 8.12). Congenital defects are present right from the birth. They occur due to an insult to the developing heart. The risk of a child being born with a congenital heart defect in general population and with a positive family history is given in Box 8.1. Acquired heart defects are seen to occur in a heart which was normal at birth.

Congenital Cardiovascular Disorders

These are classified as structural cardiac defects (acyanotic and cyanotic), functional cardiac defects (arrhythmia) and positional cardiac defects (dextrocardia).

Structural Cardiac Defects

These are anatomical defects in the structure of heart and are further classified as acyanotic and cyanotic cardiac defects (Fig. 8.13).

BOX 8.1 Risk of congenital heart disease

- Incidence of congenital heart diseases in general population is approximately 8/1000 live births.
- If one sibling is affected, the chance of the second child having congenital heart diseases is 4%. This means that the chances of the second child being born with congenital heart disease to parents already having one similarly affected child are 4 out of 100.
- If more than two siblings are affected or one parent is affected, there are 25%–30% chances of congenital heart diseases in subsequent child. This means that the chances of the subsequent children being born with congenital heart disease to parents already having two or more similarly affected children are 25–30 out of 100.
- In cases of two or more children with congenital heart diseases, the environmental factors leading to congenital heart diseases should be ruled out.

Acyanotic. These are the defects in the heart which do not manifest with cyanosis. They can be further classified according to the presence or absence of a connection between both sides of the heart. When a communication is present between the right and left sides of the heart, the condition is classified as cardiac defect with a shunt. In the absence of such a communication, it is classified as cardiac defect without a shunt.

Cyanotic. Cyanotic cardiac defects are defects in the heart which clinically present with central cyanosis.

Functional Cardiac Defects

This includes rhythm disorders. Arrhythmias are abnormalities in the heartbeat and may be congenital or acquired. The arrhythmias are classified by the site where the impulses originate such as atrial, AV nodal and ventricular. Some of these are as follows:

1. Rhythms originating in the atrium
   - Premature atrial contractions
   - Atrial tachycardia (supraventricular tachycardia [SVT])

TABLE 8.21 Manoeuvres of Dynamic Auscultation and Their Significance

Manoeuvre	Physiological Changes	Effect on Auscultation Findings
Inspiration—take a deep breath and hold the breath	Intrapleural and intrathoracic pressures decrease Flow to the right side of heart from SVC and IVC increases	Murmurs originating in the right side (e.g., TR, PS) become more prominent due to increased volume or flow
Expiration—breath out and hold the breath	Intrapleural and intrathoracic pressures increase Flow from SVC and IVC decreases, decreasing the flow to the right side of the heart. Flow to the left side of heart increases. Stroke output of left heart increases	Murmurs originating in the left side (e.g., MS) become more prominent during expiration
Left lateral position	Mitral valve becomes closer to the chest wall	MDM of MS is heard better
Lying down from sitting position	Change in the position of the neck will relieve the obstruction due to the kinking of vein at the transverse process of atlas	Decreases the venous hum
Leaning forwards	Aortic valve becomes closer to the chest wall	Murmurs originating in the aortic valve become more prominent. EDM of AR will be heard better
	Pericardium becomes more close to the chest wall	Pericardial rub will be heard better in this position.
Breath holding in any phase of respiration	Movement of pleura stops	This will decrease the rub due to pleuritis whereas rub due to pericarditis will persist
Pressing the stethoscope on chest	Pleural movement decreases	The pleural rub decreases and pericardial rub is heard better
Squatting/Valsalva (Attempt forced expiration in closed glottis when the mouth is shut and the nose is held closed.)	It causes decreased inflow to the right side of the heart thereby decreasing the ventricular volume or ejection fraction	Murmur of HOCM will be heard louder due to close opposition of ventricular walls causing more obstruction Murmur of MVP increases MVP click moves closer to S_1 due to more redundancy of chordae tendinae ESM of AS will be decreased by Valsalva manoeuvre
Muller manoeuvre—forced inspiration is attempted against a closed glottis by closing the nose and mouth	This decreases the intrathoracic pressure thereby increasing inflow into the left side of the heart and decreasing flow to the left side of the heart	Murmur of MVP decreases during this manoeuvre. Murmurs originating on the right side will increase whereas the murmurs originating on the left side will become soft
Isometric hand grip—interlock the hooked fingers of both hands and try to pull the hands against each other without change in the length of the muscles	Increases the systemic vascular resistance	Murmurs of regurgitation (MR,VSD) will become louder due to back pressure whereas murmur of AS becomes softer due to decreased gradient across the valve
Transient arterial compression	It has the same effect as isometric hand grip	It has the same effect as isometric hand grip
Standing to squatting or passive leg raise	It increases the blood return and increases systemic vascular resistance	HOCM murmur becomes softer due to increased diastolic volume MVP click moves away from S_1 due to tighter chordae tendinae
Exercise—ask the child to run for a short distance	There will be increased flow through the valves	MS murmur is heard better Intensity of PS murmur will be increased
Standing	HOCM murmur will become louder and MVP murmur will be lengthened and intensified	Most other murmurs will be decreased

AR—aortic regurgitation, EDM—early diastolic murmur, HOCM—hypertrophic obstructive cardiomyopathy, IVC—inferior vena cava, MDM—middiastolic murmur, MR—mitral regurgitation, MS—mitral stenosis, MVP—mitral valve prolapse, PS—pulmonary stenosis, SVC—superior vena cava, TR—tricuspid regurgitation, VSD—ventricular septal defect.

TABLE 8.22 Dynamic Auscultation in Various Cardiac Conditions

Condition	Murmur Heard Better	Murmur Becomes Soft
Aortic stenosis (ejection systolic murmur)	Inhalation of amyl nitrate, patient lying down or squatting	Valsalva manoeuvre
Aortic regurgitation	Early diastolic murmur of aortic regurgitation increases on leaning forwards, holding breath in expiration and with handgrip exercises Austin Flint murmur will be heard better during isometric exercise or with vasopressor (phenylephrine)	Inhalation of amyl nitrate Valsalva manoeuvre
Venous hum—continuous murmur, louder in diastole	Chin turned upwards and to opposite side During inspiration Best heard with patient sitting upright	Reduced or abolished by digital compression of the ipsilateral internal jugular vein Valsalva manoeuvre Recumbency (supine position) Turning the head to midline
Systolic murmur of hypertrophic obstructive cardiomyopathy	Valsalva	Passive leg raise Ask the child to rise from squatting position to standing position
Pericardial rub	Leaning forwards, firm stethoscope, respiration held in expiration	Lying down supine
Mitral stenosis (middiastolic murmur)	With *b*ell of the stethoscope during *e*xpiration with the patient *l*ying down in *l*eft lateral position (remember with mnemonics—BELL)	Valsalva maneuver will decrease the intensity of diastolic murmur due to decrease in pressure gradient between left atrium and left ventricle
Mitral regurgitation (pansystolic murmur)	Exercise Isometric hand grip	During inspiration Sudden standing Amyl nitrate inhalation
Mitral valve prolapse syndrome	On standing and inhalation of amyl nitrate, the click and the onset of murmur occurs earlier. This is because of decreased blood flow to the right ventricle	On raising of legs, squatting, isometric contraction, prone position and expiration, the click and the onset of murmur is delayed. This is due to increased blood flow to the right ventricle

- Atrial fibrillation
- Atrial flutter

2. Disturbances of sinus node function
   - Sinus tachycardia
   - Sinus bradycardia
   - Sinus arrythmia
   - Sick sinus syndrome
3. Rhythms originating in the AV node
   - Nodal premature beats
   - Nodal or junctional rhythm
   - Nodal tachycardia (SVT)
4. Ventricular arrhythmias
   - Premature ventricular contraction
   - Ventricular tachycardia
   - Ventricular fibrillation

Positional Cardiac Defects

The heart can be viewed as three separate segments, namely great vessels, atria and the ventricles. The position of these may vary alone or together. The abnormalities can be seen in any of the following:

1. *Position of atria:* The right atrium normally lies on the same side as the liver and on the opposite side of the stomach. The sinoatrial (SA) node is always present on the right atrium.
   (a) *Situs solitus:* The right atrium lies to the right of the left atrium. The *P*-axis in ECG denotes the site of SA node. It lies in the right lower quadrant between 0° and +90°.

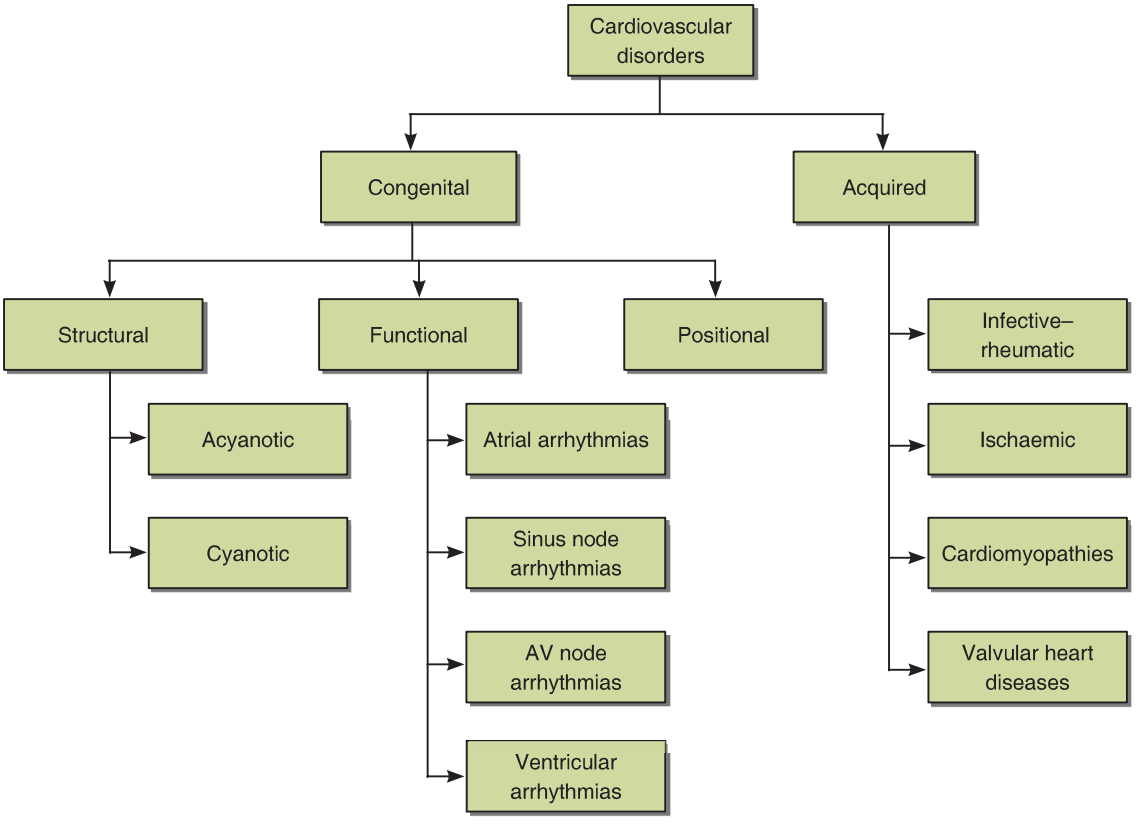


FIGURE 8.12 Classification of cardiovascular disorders.

(b) *Situs inversus:* The right atrium lies to the left of the left atrium. The *P*-axis lies in the right lower quadrant between +90° and 180°.

2. *Position of ventricles:* During the development of the heart, the straight heart tube bends to the right forming a D-loop, thereby the anatomic right ventricle lies to right of left ventricle. If the heart tube bends to the left it is called as L-loop, thereby the anatomic right ventricle lies to left of left ventricle.
3. *Position of great arteries:* The relationship between the two major arteries, that is aorta and pulmonary artery, and the relationship between the two arteries and the ventricles should be assessed by ECHO.
   (a) *Solitus:* The aortic valve is on the right and posterior to the pulmonary valve. This is the normal position and is known as situs solitus.
   (b) *Inversus:* The aortic valve is posterior and leftward to the pulmonary valve.
   (c) *D-transposition:* The aortic valve is anterior and to the right of the pulmonary valve.
   (d) *L-transposition:* The aortic valve is anterior and to the left of the pulmonary valve.
4. *Position of the heart:* Position of the heart as a whole is denoted by the following terms:
   (a) *Mesocardia:* The heart is located in the midline in the thorax.
   (b) *Levocardia:* The heart is on the normal position (left side) but the related organs are on the wrong side. It is seen in conditions such as corrected transposition of great vessels or situs inversus.
   (c) *Dextrocardia:* The heart is located on the right side of the thorax. It is of the following types:

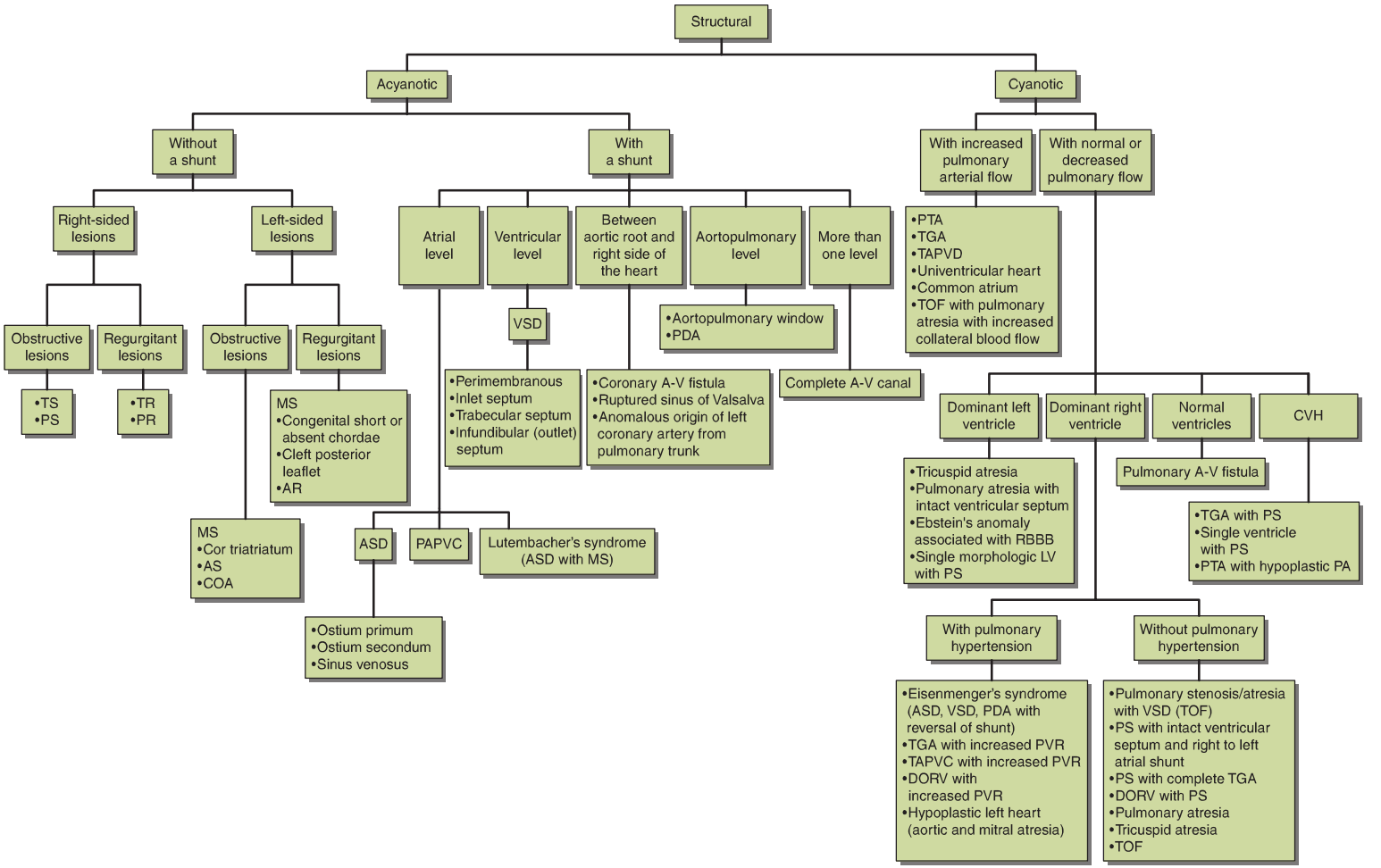


FIGURE 8.13 Structural cardiac defects. *Abbreviations*: AR—aortic regurgitation, AS—aortic stenosis, ASD—atrial septal defect, COA—coarctation of aorta, CVH—combined ventricular hypertrophy, DORV—double outlet right ventricle, LV—left ventricle, MR—mitral regurgitation, MS—mitral stenosis, PA—pulmonary artery, PAPVC—partial anomalous pulmonary venous connection, PHT—pulmonary hypertension, PR—pulmonary regurgitation, PS—pulmonary stenosis, PTA—persistent truncus arteriousus, PVR—pulmonary vascular resistance, RBBB—right bundle branch block, TAPVD—total anomalous pulmonary venous drainage, TGA—transposition of great arteries, TOF—tetralogy of Fallot, TR—tricuspid regurgitation, TS—tricuspid stenosis, VSD—ventricular septal defect, PDA—patent ductus arteriosus.

- Exact mirror image dextrocardia.
- Normal heart displaced to the right side, also known as dextroversion where the normal right to left side relation is maintained.
- Congenitally corrected TGA with situs solitus.
- Single ventricle.

Acquired Cardiovascular Disorders

These disorders occur in a heart which was normal at birth. The causes can be classified as follows:

1. Cardiovascular infections
   - Infective endocarditis
   - Myocarditis
   - Pericarditis
   - Acute rheumatic fever
   - Kawasaki's disease
   - Chaga's disease
2. Cardiomyopathies—drug-induced cardiomyopathy (antimalignant drugs such as adriamycin [doxorubicin])
3. Valvular heart diseases—right-sided PS, pulmonary regurgitation, tricuspid stenosis, tricuspid regurgitation; left-sided MS, MR, aortic valve stenosis, AR
4. Ischaemic (not common in children)

VENTRICULAR SEPTAL DEFECT

Ventricular septal defect is the commonest congenital defect. It is a defect in the ventricular septum, leading to a communication between the right ventricle and the left ventricle.

EMBRYOLOGY

The interventricular septum consists of two parts—the muscular and membranous septa. The muscular interventricular septum develops as an outgrowth from the floor of the primitive ventricle and grows towards the endocardial bar. Growth of the septum ceases when it reaches the endocardial bar leaving an aperture, that is, the interventricular foramen. The floor of this opening is formed by the endocardial bar. This opening will be closed by the membranous septum, which develops as an outgrowth from the endocardial bar and the endocardial ridges.

The closure of the interventricular foramen is dependent on the following three factors:

1. Continued growth of the connective tissue situated on the crest of the muscular septum
2. Downward growth of the ridges dividing the conus and the truncus arteriosus
3. Projections from the atrioventricular canal from the right-sided cushions

Isolated VSD may result from faulty growth of the right-sided cushions. The common form of interventricular septal defect is due to maldevelopment of the membranous septum which results in a high or membranous VSD. The proximal part of this defect is formed by the roots of the pulmonary artery and the aorta. Less commonly, the defect is situated in the muscular septum (known as muscular VSD). Ventricular septal defects vary from a few millimetres in diameter to a defect so large that there is virtually no interventricular septum (single ventricle).

CLASSIFICATION

I. According to the number

1. *Single VSD*—there is a single defect in the interventricular septum (membranous or muscular), resulting in communication between both the ventricles (Fig. 8.14).
2. *Multiple (Swiss-cheese type) VSD* is associated with multiple fenestrations in the ventricular septum (Fig. 8.15).

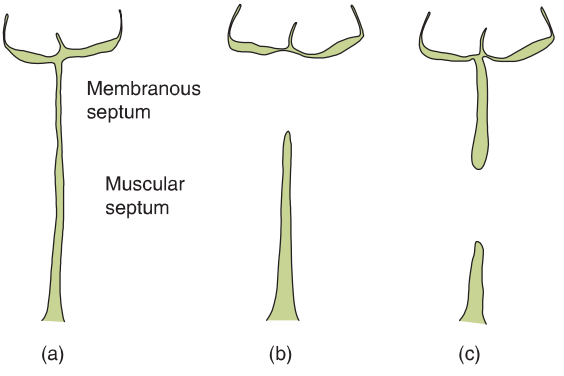


FIGURE 8.14 (a) Normal interventricular septum. (b) High membranous VSD. (c) Muscular VSD.

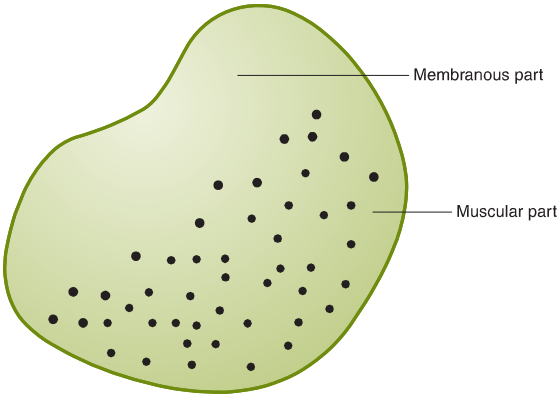


FIGURE 8.15 Swiss-cheese VSD: Multiple fenestrations in the muscular part of ventricular septum viewed with the left ventricular wall removed.

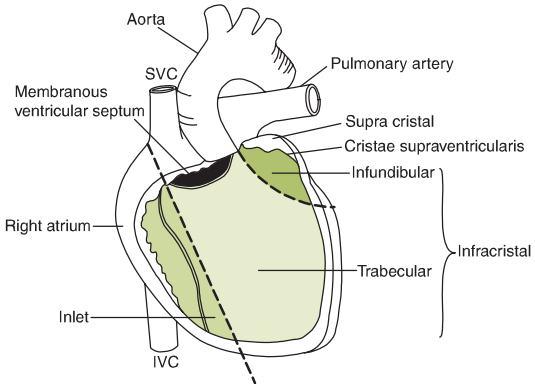


FIGURE 8.16 Sites of VSDs as seen with the right ventricular wall removed.

II. According to the size

1. *Small VSD* is less than 0.5 cm^2/m^2 of the body surface. It is known as *maladie de Roger*. In this type of VSD, haemodynamic changes are not significant. These defects usually close spontaneously.
2. *Moderate VSD* is 0.5–1 cm^2/m^2 of the body surface. The diameter is usually less than half of the diameter of the root of aorta.
3. *Large VSD* is more than 1 cm^2/m^2 of the body surface. The diameter is usually more than half of the diameter of the root of aorta and defects are non-restrictive (large defect >50% of the aortic diameter, large shunt >2.5 times the systemic flow).

III. According to the site (Fig. 8.16)

1. *Supracristal*—the defect lies above the cristae supraventricularis.
2. *Infracristal*—the defect lies below the cristae supraventricularis. These defects can be further classified as follows:
   - Membranous defect lies in the membranous part of the interventricular septum. Perimembranous defects involving the adjacent muscular septum are most common.
   - Muscular defect lies in the muscular part of the interventricular septum. Muscular VSD is of the following types—inlet, trabecular (central, apical, marginal) and infundibular (outlet).

IV. According to the flow in the VSD

1. *Restrictive VSD* is less than 0.5 cm^2/m^2 of the body surface. This defect closes as the ventricle contracts during systole. Hence, the murmur is heard only in the early part of the systole. The risk of development of pulmonary hypertension is low.
2. *Non-restrictive VSD* is more than 1 cm^2/m^2 of the body surface. This defect does not close as the ventricle contracts during systole. Hence, the murmur is heard throughout the systole. The risk of development of pulmonary hypertension is high.

ASSOCIATED DEFECTS

Ventricular septal defect may be isolated or associated with other congenital cardiac defects. These are given below:

- Pulmonary stenosis (most common)
- Truncus arteriosus
- Tetralogy of Fallot
- Common atrioventricular canal
- Double outlet right ventricle (DORV)
- Eisenmenger's complex
- Tricuspid atresia
- Valvular pulmonary stenosis
- Corrected TGA
- Coarctation of aorta
- Other shunts such as ASD and PDA
- Obstructive lesions such as subaortic stenosis

stenosis and mitral stenosis
- Incompetent atrioventricular valves

CONDITIONS ASSOCIATED WITH VSD

Ventricular septal defect may be associated with many conditions as given below:

1. Chromosomal anomalies
   - Trisomy 21 (Down's syndrome)
   - Trisomy 18 (Edward's syndrome)
   - Trisomy 13 (Patau's syndrome)
   - Cri-du-chat syndrome (deletion 5p)
   - Deletion 4p
   - XXXXX (penta X syndrome)
   - 10q-, 13q- and 18q-
   - Triploidy
   - Trisomy 9
2. Syndromes
   - Cornelia–de–Lange syndrome
   - Klippel–Feil syndrome
   - Cardiofacial syndrome
   - Foetal alcohol syndrome
   - CHARGE syndrome
   - Foetal hydantoin syndrome
   - Apert's syndrome
   - Ellis–van Creveld syndrome
   - Rubinstein–Taybi syndrome
   - Meckel–Gruber syndrome
   - Smith–Lemli–Opitz syndrome
   - Treacher–Collins syndrome
   - Velocardiofacial syndrome
   - Conradi–Hunermann syndrome
   - VATER syndrome
   - Crouzon's syndrome
   - Holt–Oram syndrome
3. Maternal conditions
   - Diabetes
   - Phenylketonuria
4. Teratogenic agents
   - Alcohol
   - Hydantoin
   - Valproate
   - Trimethadone

HAEMODYNAMICS

The right ventricular pressure is usually one-fifth of the left ventricular pressure. This causes a pressure gradient across the VSD. The direction of shunt depends on the pressure gradient. The magnitude of shunt depends on the size of the defect and the level of pulmonary vascular resistance (PVR). Based on this, VSD can be classified into four anatomic-physiologic groups. Subsequent discussion in this section is based on these groups:

- Small VSD with low PVR
- Moderate VSD with variable PVR
- Large VSD with moderate elevation of PVR (hyperkinetic pulmonary hypertension)
- Large VSD with marked elevation of PVR

In small VSD, the left-to-right shunt does not depend on PVR as the defect is small and resistance is high at the level of defect. The flow across the shunt is not significant. There will be only a loud murmur due to shunt. There is no cardiomegaly and the P_2 and ECG will be normal. X-ray will show a normal-sized heart with or without slight increase in pulmonary blood flow.

In moderate and large VSD, flow depends on PVR as the resistance at defect is minimal. Moderate VSD is associated with a systolic pressure difference of 15 mm Hg or more between the ventricles during ventricular ejection. In large VSD, the systolic pressure in both the ventricles approximates each other and the shunt is non-restrictive. Marked elevation of PVR is not seen in moderate VSD.

In a newborn with large VSD, CHF does not occur till 6–8 weeks until the PVR drops to a significant level and the flow in the shunt increases.

In moderate-to-large VSD, there will be increased shunting of the blood across the VSD. The right ventricle is in systole when the flow through the VSD enters the right ventricle. This results in increased flow of blood directly into the pulmonary artery. The right ventricle is prevented from volume overload. The blood flow into the left side of the heart is increased. This explains the fact that LVH occurs earlier than the RVH. There will be enlargement of main pulmonary artery, left atrium and left ventricle. As a protective mechanism to prevent pulmonary congestion, there will be an increase in the pulmonary artery pressure.

This pulmonary hypertension will cause RVH. P_2 is loud due to pulmonary artery hypertension.

In an untreated large VSD, irreversible changes occur in pulmonary arterioles, which lead to development of pulmonary vascular obstructive disease (POVD) (Eisenmenger's syndrome). Due to marked elevation of PVR, the left-to-right shunt decreases and there is reduction in the size of left ventricle and overall size of the heart. The pulmonary artery segment remains prominent and features of RVH can be seen.

CLINICAL FEATURES

These depend on the size of the defect.

1. Small VSD—the child is asymptomatic, has normal growth and development and is diagnosed during routine check-up
2. Moderate-to-large VSD—the child presents with the following features:
   - Exercise intolerance
   - Delayed growth/poor weight gain
   - Features of CCF
   - Recurrent respiratory tract infections
   - Cardiomegaly
3. Large VSD with marked pulmonary hypertension (reversal of shunt—Eisenmenger's syndrome)
   - Cyanosis
   - Clubbing
   - Polycythaemia

General Examination Findings

1. Pulse
   - Small VSD—normal
   - Moderate VSD—normal or brisk
   - Large VSD with CCF—pulsus alternans
2. Jugular venous pressure
   - Usually normal
   - Increased with large VSD with CCF

Cardiac Examination Findings

1. Inspection findings
   (a) Small VSD—normal
   (b) Moderate VSD—moderate parasternal lift
   (c) Large VSD—hyperdynamic precordium
   (d) Eisenmenger's syndrome—the hyperdynamic activity of the precordium will be absent because the left ventricular workload approximates normal
2. Palpatory findings
   (a) Small VSD—normal
   (b) Moderate and large VSD
   - Precordium—prominent (in cardiomegaly)
   - Parasternal heave (in right ventricular hypertrophy)
   - P_2 is palpable (in pulmonary hypertension)
   - Thrill (systolic) along the left sternal border
3. Auscultation findings
   (a) Small VSD
   - Second heart sound is normal
   - Loud pansystolic murmur along the left sternal border with/without a thrill. Murmur may be soft and only early systolic in timing (Fig. 8.17). (Murmur is harsh in quality. This is because the orifice is fixed and the turbulence is created by the high velocity of flow through the opening.)
   - There are no flow murmurs across the mitral valve

   (b) Moderate VSD
   - S_1 will be loud at the apex, due to increased left ventricular end diastolic volume and workload
   - Second sound is often widely split with normal or slight increase in the intensity of P_2. As the PVR increases, the degree of the split decreases. The second sound remains split in expiration
   - P_2 is loud (due to increased pulmonary blood flow in the absence of increased pulmonary pressure)
   - Occasionally a third heart sound (S_3) may be heard over the apical region (due to augmentation of filling of the ventricle). This S_3 is flow-related
   - Murmur grade will be 4–6 (loud, harsh, holosystolic murmur, associated

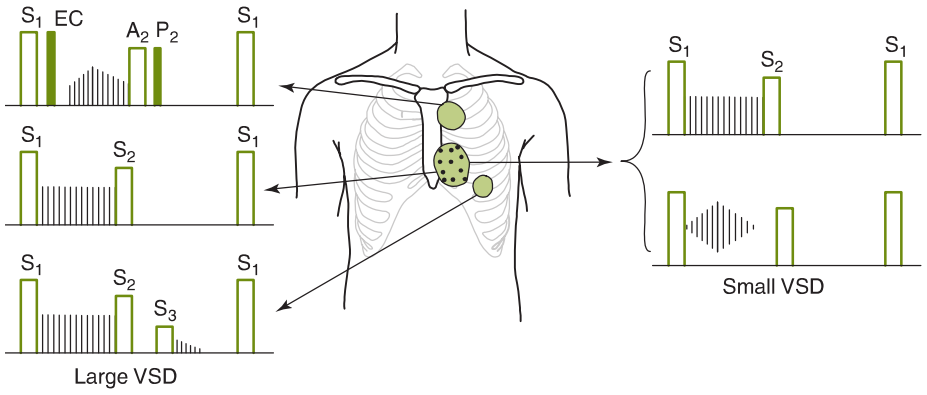


FIGURE 8.17 Auscultation findings in VSD. Thrill is represented by dotted area at the lower left sternal border.

with thrill). The murmur is holosystolic (throughout the systole) due to a continuous pressure gradient across the defect. It is best heard along the left sternal border. It also signifies that the right ventricular pressure is significantly less than the left

- Soft, short, systolic murmur in the second left ICS (due to the pulmonary hypertension)
- A middiastolic flow murmur is heard in the mitral valve area due to increased blood flow across the mitral valve
- Early diastolic murmur due to pulmonary regurgitation (Graham Steell murmur) will be heard at a later stage when severe pulmonary hypertension develops

(c) Large VSD with moderate increase in PVR (Fig. 8.17)

- S_2 is loud and closely split with a loud P_2 component
- Loud pansystolic murmur with thrill at the lower left sternal border. It may disappear during the latter third of the systole before the closure of the aortic valve
- S_3 will be heard
- Middiastolic rumble will be heard in the left ventricular apical area (moderately loud and long)
- Murmur in the upper-left parasternal area due to ejection of blood into the pulmonary artery or mild functional infundibular stenosis
- Pulmonary ejection systolic murmur may be preceded by an ejection click
- Early diastolic murmur as a result of mild pulmonary insufficiency

(d) Large VSD with marked increase in PVR

- With the development of pulmonary hypertension the loud systolic murmur decreases and a marked degree of RVH occurs
- The patient may appear normal (quiet heart, loud S_2, insignificant murmurs; bidirectional shunting across the defect in various phases of the cardiac cycle). The absence of murmurs can be accounted for by the relative small flow across the defect which fails to generate sufficiently high velocity to create the turbulence
- S_3 may be heard
- The P_2 is loud and palpable
- Systolic murmur may be short or absent
- Pulmonary ejection systolic murmur will be heard in the pulmonary area
- No diastolic rumble will be heard in the left ventricular apical area

NATURAL HISTORY

- Spontaneous closure occurs in VSD. It occurs more frequently in small defects and more often in the first year of life than thereafter. Large defects tend to become smaller with age.
- Some infants with large VSD may develop infundibular stenosis resulting in decreased left-to-right shunt. It may even produce right-to-left shunt in some cases.
- Congestive cardiac failure develops in infants with large VSD. It usually does not occur until 6–8 weeks of age.
- Pulmonary vascular obstructive disease may begin to develop as early as 6–12 months of age in patients with untreated large VSD, but right-to-left shunt usually does not develop until the second decade of life.

Spontaneous Closure

Ventricular septal defect closes spontaneously when the defect is perimembranous or in the muscular septum and the size is small (diameter of <0.5 cm^2/m^2 of the body surface). The infundibular type usually does not close spontaneously.

Mechanism of Spontaneous Closure

- Approximation of the edges of the VSD
- Hypertrophy of the septal muscle around the defect
- Closure by the ventricular septal aneurysm
- Prolapsed aortic valve leaflet may close the VSD
- Prolapsed tricuspid valve leaflet
- Fibrous tissue proliferation
- Endocardial proliferation

DIFFERENTIAL DIAGNOSIS

In the following conditions the clinical picture will mimic an isolated VSD.

- Truncus arteriosus with increased pulmonary blood flow without overt cyanosis may be mistaken for VSD.
- Mild or moderate subaortic stenosis.
- Corrected transposition of great vessels with VSD.
- Common ventricle without PS.

INVESTIGATIONS

1. ECG

(a) Small VSD—normal

(b) Moderate VSD with decreased or normal PVR

- Left axis deviation
- Left atrial enlargement—broad, notched p (biphasic P waves in leads I, aVR and V_6)
- Left ventricular enlargement—tall R in leads I, II and aVF
- P-R interval normal or slightly prolonged
- Prominent Q and tall R in V_5 and V_6

(c) Large VSD

- Right axis deviation
- Biventricular enlargement—tall R in V_1, deep Q in V_5 and V_6
- Midprecordial leads (V_3/V_4) show equiphasic RS complexes
- RBBB may be seen

(d) Large defects with marked elevation of PVR (essentially normal work done by left ventricle)

- Evidence of left ventricle and left atrial enlargement is absent
- QRS pattern in lead V_1 due to RVH

2. Chest X-ray

(a) Small VSD—normal

(b) Moderate VSD—mild-to-moderate cardiac enlargement, mild prominence of the pulmonary artery and increase in the pulmonary vasculature

(c) Large VSD—significant cardiomegaly with left atrial enlargement (in lateral view)

- Right atrial enlargement (with CCF)
- Dilated main pulmonary artery and prominent pulmonary conus
- Pulmonary plethora

(d) Eisenmenger's complex

- Minimal cardiomegaly
- Oligaemic lung fields with central plethora
- Left atrium/ventricle normal
- Moderately dilated pulmonary trunk

3. ECHO—the site and size of the defect can be visualised.

(a) Exaggerated mitral valve motion

(b) Pulmonary stenosis and pulmonary hypertension are detected

4. Cardiac catheterisation

(a) Visualisation of the catheter—the catheter may be passed through the septal defect and visualised in the left ventricle

(b) Oxygen studies—samples of blood from the right ventricle and the pulmonary artery show higher percentage of oxygen saturation than samples from the vena cava and the right atrium

(c) Pressure studies—the pressure in the right ventricle and the pulmonary artery may be increased. Pulmonary entry pressure is at systemic level in large VSD

5. Doppler study detects the direction of blood flow across the shunt. Pulmonary to systemic blood flow ratio will be around 2:1 in moderate VSD and above that in large VSD. Little turbulence occurs across the defect in large VSD as the pressure in the ventricles is nearly equal

6. Selective right ventriculogram shows simultaneous opacification of both the ventricles

TREATMENT

Medical

1. Small VSD:

- When the Q_P:Q_S ratio is less than 1.5:1, observe the patient for spontaneous closure. No treatment is needed. These children should be followed up.
- Even a VSD less than 0.2 cm^2/m^2 of the body surface will predispose to infective endocarditis. So observe for the complications.

2. Moderate VSD:

- Likely to close spontaneously.
- Observe for pulmonary hypertension. Plan for surgical closure of VSD by 2–5 years or earlier if the child shows evidence of increase in the pulmonary pressure (Q_P:Q_S ratio is more than 1.8:1).
- Antifailure treatment is given if the child presents with CCF.

3. Large VSD with hyperkinetic pulmonary hypertension:

- Chance for closure is low.
- In absence of complications, observe for 6–9 months. At 6 months, if the VSD is still large, plan for closure immediately or else plan closure by 2–5 years.
- If the pulmonary pressure is more than 50% of the systolic pressure or if the child develops CCF, infective endocarditis or growth failure, surgical closure is indicated.
- Antifailure treatment is given.

4. Large VSD with high PVR:

- It is better to prevent the development of Eisenmenger's syndrome by early diagnosis of pulmonary hypertension and early surgical closure of large VSD.
- Pulmonary vascular resistance in the basal state and after pulmonary vasodilator such as nitric oxide should be measured. Surgery is possible when the fall in PVR is 6 units or more (reversible pulmonary hypertension). Patients with irreversible pulmonary hypertension cannot be operated. In such cases, advice should be given regarding regulation of activities and avoidance of stress.
- Heart–lung transplantation is the only option available for inoperable cases.

Surgical

The ideal age for surgical closure is below 2 years.

- Small VSD—it should be treated immediately if associated with other cardiac defects (doubly committed), lest aortic incompetence develops.
- Moderate VSD—plan for surgical closure of VSD by 2–5 years. It is done when the child shows evidence of increase in pulmonary pressure.
- Large VSD with hyperkinetic pulmonary hypertension—if the VSD is large, plan for closure immediately or else plan closure by 2–5 years.
- Large VSD with high PVR—some children are still operable. These children should be operated. Heart–lung transplantation is the only option available.

Indications

- Development of pulmonary hypertension
- Pulmonary to systemic flow rate is >1.5:1
- Congestive failure not responding to medical

treatment
- Infective endocarditis
- Large VSD
- When associated with other cardiac defects

Contraindications

- Development of irreversible pulmonary hypertension
- Eisenmenger's complex
- In older patients, a large VSD and a left-to-right shunt of 1.5–1.8 at rest that becomes 1 or less during moderate exercise
- Significant fall in arterial saturation during exercise

Complications

- Conduction blocks
- Residual VSDs
- Surgical risks are higher for Swiss-cheese type of VSD

COMPLICATIONS

- Congestive cardiac failure
- Infective endocarditis
- Pulmonary hypertension
- Eisenmenger's complex (reversal of shunt)
- Recurrent respiratory infections
- Paradoxical embolism
- Failure to grow
- Haemoptysis—incidence of haemoptysis increases with age

The complications vary with the type of the VSD.

- In small VSD, infective endocarditis is common. The incidence of this is low in trabecular type of the defects.
- In moderate VSD with decreased or variable PVR, congestive cardiac failure is common.
- In large VSD, congestive cardiac failure with prolonged pulmonary vascular disease is common.

FOLLOW-UP

In a case of VSD, if the child becomes better without the treatment consider the following possibilities:

- Restrictive VSD
- Acquired pulmonary infundibular stenosis
- Development of pulmonary hypertension

PROGNOSIS

Sudden improvement of symptoms of VSD may be due to spontaneous closure of VSD or development of PS. Some children with supracristal VSD may develop AR.

1. *Small VSD*—most of these defects close spontaneously. Usually not associated with CCF and pulmonary hypertension.
2. *Moderate VSD*—some of these defects close spontaneously or become smaller.
3. *Large VSD with hyperkinetic pulmonary hypertension* (moderate increase in PVR)—the risk of early POVD is high.
4. *Large VSD with marked increase in PVR*—the prognosis is poor once the symptoms appear. Patients die of CCF and haemoptysis.

Differences between the four anatomic–physiologic groups of VSD are summarised in Table 8.23.

ATRIAL SEPTAL DEFECT

It is a congenital cardiac disease, where there is a defect in the interatrial septum. This results in an abnormal communication between both the atria. The defect usually occurs in isolation.

EPIDEMIOLOGY

- Incidence—atrial septal defect constitutes approximately 10% of all congenital heart diseases.
- Gender—it is more common in females. Female to male ratio of ASD is 2:1.
- Age—it is a congenital heart disease, but it usually manifests in adults.

EMBRYOLOGY

The atrium develops from a common atrial canal. It is divided into right and left atria by the downward growth of a septum (Fig. 8.18). This is called *septum primum*. As this septum grows downwards,

TABLE 8.23 Showing the Differences between the Four Anatomic–Physiologic Groups of VSD

Features	Small VSD (with Low Pulmonary Vascular Resistance)	Moderate VSD (with Variable Pulmonary Vascular Resistance)	Large VSD with Moderate Elevation of PVR (Hyperkinetic PHT)	Large VSD with Marked Elevation of PVR
Size	<0.5 cm^2/m^2 of the body surface	0.5–1 cm^2/m^2 of the body surface <½ the diameter of the root of aorta	>1 cm^2/m^2 of the body surface >½ the diameter of the root of aorta	>1 cm^2/m^2 of the body surface
Haemodynamic changes	Mild changes	Moderately large left to right shunts	Equal right and left ventricular systolic pressures	Shunt bidirectional or right to left Normal to decreased pulmonary blood flow
PHT	Not present	Mild to moderate	Moderate elevation	Marked elevation
Symptoms	Asymptomatic	Growth retardation CCF unusual	Feeding difficulties Growth failure Increased forehead sweating	Patients appear healthy, compensated heart Rarely cyanosis, syncope, arrhythmia, sudden death can occur
Signs	Thrill +	Thrill + Hyperdynamic left ventricular lift	Hyperdynamic precordium, tachypnoeic, JVP elevated (*a* and *v* waves accentuated) Parasternal heaving	Quiet heart S_2 loud
Auscultation				
Heart sounds	S_1 normal S_2 split	S_2 widely split S_3 at apex S_1 may be loud P_2 loud (increased pulmonary flow)	S_2 closely spilt P_2 loud	Quiet heart S_2 loud S_2 single or closely spilt
Murmur	Harsh, loud (Grade IV–VI) pansystolic murmur (only early diastolic) maladie de roger No flow murmur across the mitral valve	Flow murmur at the apex (MDM)	Short, early systolic murmur Early systolic murmur MDM at apex	No murmur of VSD Insignificant murmurs. EDM of PR (Graham Steell's murmur) No MDM at apex
Investigations				
ECG	Normal No cardiomegaly	RAD Prolonged P-R interval P mitrale (left atrial enlargement Normal or LVH, no RVH	Biventricular hypertrophy Left atrial enlargement-P pulmonale Deep Q in V_5, V_6	RVH RAD P wave normal Tall R wave in V_6 arrhythmias

(Table continued)

TABLE 8.23 *(Continued)*

Features	Small VSD (with Low Pulmonary Vascular Resistance)	Moderate VSD (with Variable Pulmonary Vascular Resistance)	Large VSD with Moderate Elevation of PVR (Hyperkinetic PHT)	Large VSD with Marked Elevation of PVR
X-ray	Normal or slightly increased vascularity Borderline cardiac enlargement	Mild-to-moderate cardiomegaly Increased pulmonary vascular makings (both central and peripheral lung fields)	Cardiomegaly Pulmonary plethora Increased pulmonary vascular markings (Both central and peripheral lung fields) Left atrial enlargement Prominent main PA	Minimal cardiomegaly Prominent PA Central plethora Vascularity of outer third of the lung fields is reduced
Course and prognosis	Most of these defects closes spontaneously by 2 years. Prognosis is good	Some close spontaneously. Some become smaller in size	Delay in surgical closure will lead to increased morbidity and mortality	Prognosis is poor, once the symptoms start

CCF—congestive cardiac failure, ECG—electrocardiography, EDM—early diastolic murmur, EDM—early diastolic murmur, JVP—jugular venous pressure, LVH—left ventricular hypertrophy, MDM— middiastolic murmur, PA—pulmonary artery, PHT—pulmonary hypertension, PR—pulmonary regurgitation, RAD—right axis deviation, RVH—right ventricular hypertrophy, VSD—ventricular septal defect.

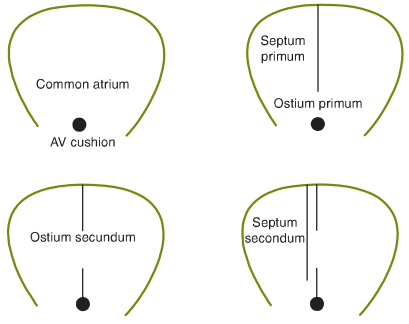


FIGURE 8.18 Development of interatrial septum.

towards the atrioventricular cushion, there is a communication between the septum primum and the atrioventricular cushion. This is called *ostium primum*. As the septum fuses with the atrioventricular cushion, the ostium primum closes. However, before the closure is complete, a defect (usually a break) occurs in this septum high above. This is called *ostium secundum*. It ensures free blood flow from the right atrium to the left atrium. At this stage, another crescent-shaped fold grows down from the roof of the right chamber. This is called *septum secundum*. It overlaps the ostium secundum. It never forms a complete partition in the atrial cavity. The opening left by the septum secundum is called foramen ovale. The upper part of septum primum gradually disappears. The remaining part becomes the valve of the foramen ovale. There remains an oblique cleft between the two atrial cavities. After birth, the pressure in the left atrium increases and the foramen ovale is obliterated. It prevents flow of blood from the left ventricle to the right ventricle. The remnant of the foramen ovale is called fossa ovalis.

Rarely, the septum may be nearly absent and result in a single functional atrium. Isolated patent foramen ovale is usually of no haemodynamic significance. But the blood can flow from the right atrium to the left if the right atrial pressure exceeds that of the left atrium.

TYPES

There are five types of ASD (Fig. 8.19).

Ostium Secundum

This type is seen most frequently. It is located at the site of fossa ovalis. It may be single or multiple. It is due to excessive resorption of septum primum or deficiency in the growth of the septum secundum.

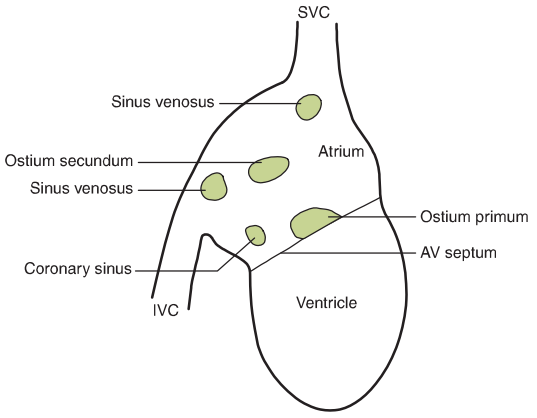


FIGURE 8.19 Sites of various types of ASD. Sinus venosus is located at the posterosuperior portion of the atrial septum. Secundum type is located at the site of fossa ovalis. Ostium primum is located near the ventricular septum. Coronary sinus type is located at the anteroinferior portion of the atrial septum at the roof of the coronary sinus.

It usually occurs in isolation. Rarely, this may be associated with mitral valve prolapse syndrome (MVPS) or MS in Lutembacher's syndrome.

One third of ostium secundum types of ASD closes spontaneously by 1–2 years of age by the downward growth of the septum secundum.

Ostium Primum

It is located in the lower portion of the interatrial septum. It may occur in isolation or may be associated with complete endocardial cushion defects, cleft mitral valve, MR and tricuspid regurgitation. This type of defect is seen in Down's syndrome. According to the associated defects, it can be complete or incomplete.

- *Complete:* ASD with MR with VSD.
- *Incomplete:* ASD with MR.

Patent Foramen Ovale

There is no structural defect in the atrial septum, but there is a functional incompetency of the valve mechanism of foramen ovale. An isolated patent foramen ovale is not significant haemodynamically and is not considered as ASD. When the right atrial pressure is increased due to other defects such as pulmonary atresia; venous blood may shunt across the patent foramen ovale. Risk of systemic embolism is present.

Sinus Venosus

This is of two types:

1. *Superior vena caval* type: It occurs high in the atrial septum near the entrance of the superior vena cava (SVC). It is small, non-restrictive and inferior to the orifice of SVC. It is usually associated with anomalous connection of the right superior pulmonary vein.
2. *Inferior vena caval* type: It is located near the entry of inferior vena cava (IVC) into the right atrium.

Coronary Sinus ASD

This type is seen least commonly. There is a communication between the coronary sinus and left atrium.

Features of common types of ASD are given in Table 8.24.

ASSOCIATED DEFECTS

1. Cardiac defects—the combination of MS (congenital or acquired, usually rheumatic) and atrial septal defect is known as *Lutembacher's syndrome*. It often manifests as CCF and atrial fibrillation in adults. This is a rare condition. Cardiac malformations are most commonly associated with ASD:
   - Partial anomalous pulmonary venous drainage
   - Pulmonary valvular stenosis
   - Ventricular septal defect
   - Pulmonary arterial branch stenosis
   - Persistent left SVC
   - Mitral valve prolapse syndrome
   - Mitral incompetence
2. Skeletal deformities such as arachnodactyly are often associated with ASD and MVPS

TABLE 8.24 Features of Common Types of Atrial Septal Defect

Features	ASD Type		
	Ostium Secundum	Ostium Primum	Sinus Venosus
Incidence	50%–70%	30%	10%
Site	At the fossa ovalis	Endocardial cushion defect inferior to fossa ovalis	SVC type above the level of atrial septum IVC type at the opening of IVC
Associated lesions	MS in Lutembacher's syndrome, MVPS	Mitral incompetence—cleft anterior mitral leaflet Tricuspid incompetence—cleft tricuspid valve	Anomalous pulmonary venous drainage, MVPS
Chest X-ray	Jug handle appearance of the heart, increased pulmonary vasculature, Hilar dance	Gross cardiomegaly, globular heart, pulmonary congestion	Figure of eight appearance
ECG	rSR' pattern, RAD, right ventricle dominance	Left axis deviation, RVH/LVH/biventricular hypertrophy	rSR' pattern, extreme RDA, indeterminate axis
Angiocardiography	Simultaneous opacification of both atria	Goose neck deformity	Simultaneous opacification of both atria
Complications	CCF—rare	CCF, recurrent respiratory infections, growth retardation	Similar to secundum type
Prognosis	Good	Bad	Good

ASD—atrial septal defect, CCF—congestive cardiac failure, IVC—inferior vena cava, LVH—left ventricular hypertrophy, MVPS—mitral valve prolapse syndrome, RDA—right axis deviation, RVH—right ventricular hypertrophy, SVC—superior vena cava.

CONDITIONS ASSOCIATED WITH ASD

Atrial septal defect may be seen as an isolated defect or may be associated with other conditions. Therefore, whenever the following conditions are seen look for ASD. On the other hand, whenever ASD is diagnosed look for the following conditions:

1. Chromosomal disorders
   - Down's syndrome (trisomy 21)
   - Deletion syndrome 5p
   - Patau's syndrome (trisomy 13)
   - Edward's syndrome (trisomy 18)
   - Klinefelter variant (49 XXXXY)
   - Triploidy
2. Syndromes
   - Holt–Oram syndrome (skeletal abnormalities—thumb with an extra phalanx, deformities of radius and ulna)
   - Ellis–van Creveld syndrome (bell-shaped chest)
   - TAR syndrome (thrombocytopenia, absent radius)
   - Congenital rubella syndrome
   - Meckel–Gruber syndrome
   - Conradi–Hunermann syndrome
   - CHARGE syndrome
   - VATER syndrome
   - Noonan's syndrome
   - Treacher–Collins syndrome
   - Foetal alcohol syndrome
   - Foetal hydantoin syndrome
   - Lutembacher's syndrome
3. Maternal conditions
   - Phenylketonuria
   - Rubella infection
4. Teratogenic agents—drugs predisposing to ASD are
   - Amphetamines
   - Hydantoin
5. Familial recurrence
   - Scimitar syndrome
   - Holt–Oram syndrome—autosomal dominant pattern
   - Ostium secundum ASD with prolonged A-V conduction—autosomal dominant pattern

HAEMODYNAMICS

The blood from SVC and IVC enters the right atrium and then flows to the right ventricle. From here the blood passes to the lungs through the pulmonary arteries. After oxygenation in the lungs, this blood enters the left atrium through the pulmonary veins (Fig. 8.20). If the ASD is relatively large, then the pressure gradient will be small. As there is a defect in the atrial septum and the pressure in the left atrium is slightly higher than the right atrium, there will be a flow of blood from the left atrium to the right atrium. As the pressure difference between both the atria is small, the flow gradient is low. Hence, there will be no murmur. This increased flow into the right atrium will lead to increased blood flow into the right ventricle and increased flow across the normal pulmonary valve. This will cause an ESM.

Wide split. The right ventricular volume will increase due to the extra flow from the left side. This will lead to increased blood flow in the pulmonary artery. Hence, the pulmonary valve closure will be delayed. At the same time the left ventricle inflow will be decreased because of this shunt. This causes an early closure of the aortic valve. This leads to a wide split in the second heart sound (A_2P_2).

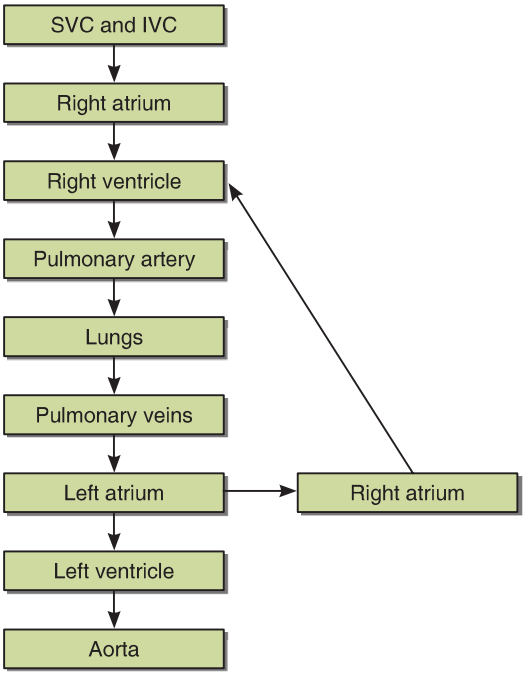


FIGURE 8.20 Haemodynamics in ASD.

Fixed split. Normally, the right atrial flow increases and the left atrial blood flow decreases during inspiration. During expiration the right atrial blood flow from the vena cava decreases and the left atrial flow increases. This occurs due to increase in the intrathoracic pressure during expiration. This results in early closure of the pulmonary valve. At the same time, the increased blood flow to the left atrium results in increased blood flow into the aorta. This results in delayed closure of aortic valve. This results in wide split during expiration. The reverse will be seen during inspiration. These differences in the atrial blood inflow during inspiration and expiration will not be present in ASD as there is a communication between the two atria. This will lead to a fixed split in the second heart sounds.

Factors leading to paucity of symptoms in infants: The symptoms start at a later age in children. They are relatively deficient in infants due to the following causes:

- Structure of the right ventricle—In early life, the muscular tricuspid valve of the right ventricle is thick and less compliant. Thus, the left-to-right shunt is limited.
- Despite the large pulmonary blood flow, the pulmonary arterial pressure remains normal because of the absence of a high pressure communication between the pulmonary and systemic circulations. The flow is from left atrium (pressure 3–6 mm Hg) to the right atrium (pressure 0–3 mm Hg).

Factors leading to the onset of symptoms in adults:

- Pulmonary vascular resistance remains low throughout childhood, although it may begin to increase in adulthood.
- The right ventricular wall becomes thinner as the child grows older due to lower pressure generating requirements. As this happens, the left-to-right shunt increases.
- Pulmonary hypertension occurs later in life. The large blood flow through the right side of the heart results in enlargement of the right atrium and right ventricle and dilatation of the pulmonary artery.

CLINICAL FEATURES

The child with ASD is usually asymptomatic, and a murmur may be detected during routine examination in the school. Secundum ASD is usually asymptomatic until the third decade of life. The common symptoms seen in ASD are

- palpitation on exertion,
- fatigue,
- dyspnoea on exertion and
- varying degrees of exercise intolerance in older children.

Rarely, ASD may present with

- growth failure,
- recurrent respiratory infections and
- congestive heart failure.

Examination of Cardiovascular System

Relevant general examination findings are as follows:

- Pulse—normal.
- Jugular venous pressure—normal in height. Crests of both *a* wave and *v* wave are equal since both atria are in communication with each other. Large *a* waves are seen when pulmonary hypertension develops.
- Physical appearance—look for features of Holt–Oram syndrome which is associated with ASD. Look for defects in the thumb or radius.

Cardiac Examination

Inspection Findings

1. Apical impulse—normal
2. Precordial movement
   - Hyperdynamic right ventricular impulse along the left sternal border due to RVH
   - Pulsatile pulmonary trunk in second left ICS

Palpation Findings

- Parasternal heave on the left side
- Pulsations in second left ICS due to dilatation of pulmonary trunk
- Systolic thrill in the pulmonary area is present if the shunt is large or if there is a coexistent PS

Auscultation Findings

1. Heart sounds

(a) First heart sound (S_1)—usually normal or may be loud due to tricuspid component.

(b) Second heart sound (S_2)—second heart sound has wide, fixed split (Fig. 8.21). The split is variable with the development of atrial fibrillation. The split is narrowed down with the development of pulmonary hypertension.

2. Murmurs (Fig. 8.21)

(a) Pulmonary ejection systolic murmur—usually grade 2–3/6 is heard in the pulmonary area due to increased flow across the pulmonary valve.

(b) Diastolic murmur—middiastolic murmur in the

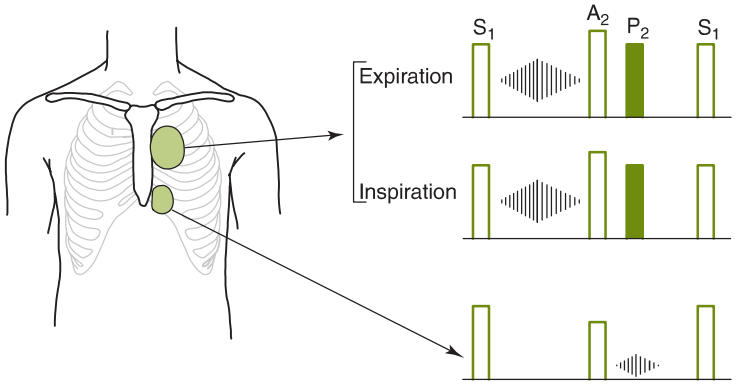


FIGURE 8.21 Auscultatory findings in ASD.

tricuspid area is due to increased flow across the normal tricuspid valve (functional tricuspid stenosis). Pulmonary regurgitant murmur (an EDM) is due to large pulmonary trunk. It is called Graham Steell murmur.

(c) Carvallo's sign—the tricuspid murmur is maximal at the lower sternal edge and increases in intensity during inspiration. With reversal of shunt, the following findings will be seen:

- Loud P_2.
- Wide fixed split narrows and disappears.
- The tricuspid MDM disappears.

DIFFERENTIAL DIAGNOSIS

Atrial septal defect should be differentiated from the following conditions:

- Pulmonary stenosis (ejection click, thrill, absence of increased pulmonary blood flow)
- High VSD (pansystolic murmur and thrill)
- Ebstein's anomaly (not associated with increased pulmonary blood flow)
- Aortic stenosis (thrill, ejection click, murmur conducted to axilla and apex)
- Idiopathic dilatation of the pulmonary artery (mimics ASD and S_2 is normally split)
- Mitral regurgitation (preferential direction of the regurgitation, for example, Gerbode defect is a ventriculoatrial defect which causes murmur in the aortic area. There is a communication between left ventricle and right atrium)

Ejection systolic murmur in the pulmonary area is present in the following conditions:

- Pulmonary hypertension (S_2 is normally split, P_2 is loud and palpable)
- Acyanotic TOF (ESM and single S_2)

Increased pulmonary blood flow occurs in the following conditions:

- Functional murmur in pulmonary area (no thrill)
- Partial anomalous pulmonary venous drainage (resembles secundum ASD but second sound is normal)
- Total anomalous pulmonary venous drainage with a large interatrial defect without pulmonary hypertension (widely split S_2, quadruple rhythm, that is, S_1, S_2, S_3 and S_4 are present)

INVESTIGATIONS

1. ECG
   (a) In ostium secundum defect
   - P-R interval prolonged
   - Right axis deviation and incomplete RBBB due to right ventricular overload
   - Right ventricular dominance—right ventricular enlargement (due to diastolic overload of right ventricle)

   (b) In Holt–Oram syndrome
   - P-R interval prolonged
   - Sinus bradycardia
   - Ectopic rhythms
   - Normal or peaked *P* wave
   - rsR' pattern in right precordial leads due to right ventricular conduction delay and RBBB. The normal impulse will produce right and left ventricular *rs* wave. A delayed right ventricular conduction will show an upward R wave after the normal conduction. This is rsR' pattern

   (c) In ostium primum defect
   - Left axis deviation
   - Incomplete RBBB
   - Complete heart block

   (d) In sinus venous type—inverted *P* in leads II, III, aVF with/without junctional rhythm
2. Chest X-ray
   (a) Cardiomegaly due to right atrial and right ventricular enlargement
   (b) Jug-handle appearance of heart due to dilated right atrium, right ventricle and pulmonary arteries with less prominent aortic knuckle
   (c) Pulmonary plethora due to increased pulmonary vascularity
   (d) Right pulmonary artery is disproportionately enlarged
   (e) Dilated pulmonary trunk
   (f) Dilated right ventricle occupies the apex
   (g) Left ventricular silhouette is seen posteriorly
   (h) Inconspicuous aortic shadow (very small aortic shadow)

(i) Dilatation of SVC in sinus venosus type
(j) Hilar dance—on fluoroscopy there is pulsation of the pulmonary arteries

3. ECHO
   (a) Location and size of ASD can be made out
   (b) Right ventricular volume overload (increased right ventricular-end diastolic volume)
   (c) Right atrial enlargement
   (d) Paradoxical movement of ventricular septum is seen in subcostal four-chamber view in echocardiography. Normally septum moves posteriorly during systole and anteriorly during diastole. In ASD, this is reversed. The sinus venosus type of ASD may require a transoesophageal echocardiography examination
4. Cardiac catheterisation—this is generally not needed
   (a) Visualisation of the catheter—the catheter may pass through the septal defect and visualised in the left atrium
   (b) Oxygen studies—samples of blood from the right atrium, right ventricle and pulmonary artery show a higher percentage of oxygen saturation than samples from the vena cava
   (c) Pressure studies—the pressure in the right atrium, right ventricle and pulmonary artery is normal or slightly increased

COURSE OF DISEASE

- Atrial septal defect is usually asymptomatic until adulthood. The symptoms develop only when the pulmonary pressure rises due to increased flow in the pulmonary artery.
- Spontaneous closure depends on the size of ASD. If the size is small, it may close as the child grows.
- Prognosis is good. Mortality rate is less than 1%.

COMPLICATIONS

1. Pulmonary hypertension due to increased pulmonary blood flow.
2. Eisenmenger's syndrome—pulmonary arterial pressure increases due to increased pulmonary blood flow. When the pulmonary hypertension increases to a pressure higher than the left side, there is a shunt of impure blood from the right side to the left at the site of defect in the atrial septum. This leads to central cyanosis.
3. Paradoxical embolism—the emboli arising from the lower limbs are filtered in the lungs in children with normal heart. In ASD, these emboli may cross the defect and enter into the systemic circulation directly. This is known as paradoxical embolism. This is prone to occur especially when embolisation is associated with a rise in the right atrial pressure.
4. Infective endocarditis occurs only if ASD is associated with other cardiac defects.
5. Congestive cardiac failure and infective endocarditis are rare in ASD. These occur when the ostium primum type of ASD is associated with other lesions such as MR or tricuspid regurgitation. Congestive cardiac failure can also occur in the following conditions:
   - If the defect is large
   - Atrial arrhythmias—atrial dysrhythmias (fibrillation, flutter) and paroxysmal atrial tachycardia
   - Ostium primum defect
   - Anomalous pulmonary venous drainage with ASD
   - Severe pulmonary hypertension leading to Eisenmenger's syndrome
   - Infective endocarditis
   - Lutembacher's syndrome
   - When associated with hypertension or coronary artery disease

TREATMENT

Medical

- Infective endocarditis prophylaxis may be given if the ASD is associated with other defects such as MVP.
- If cardiac failure is present, it should be treated.

Interventional Procedure

It involves non-surgical closure using an umbrella device.

- Transcatheter closure of ASD using occlusive devices can be done for small- to moderate-sized ASD.
- Atrial septal defect should be centrally located in the case of secundum defect if these devices are to be used.
- The defect should have at least 5-mm rim of tissue for the device to anchor it.
- Amplatzer device and clamshell double umbrella are used.
- For follow-up, aspirin (antiplatelet agent) is administered for 3 months. By this time, the raw surface of the device is expected to be fully covered by the endothelium.

Surgical Closure

The direct closure is done by a Dacron patch.

Indications

- Ostium primum defects
- Pulmonary artery pressure >50% of the systemic pressure
- Pulmonary to systemic blood flow ratio (Q_p:Q_s) of >1.5:1.
- Right ventricular volume overload
- ASD size of more than 1 cm
- All sinus venosus type
- All symptomatic ASD should be closed
- ASD with CCF

Ideal Age

The optimal age for operation is below 5 years; ideal can be considered to be 1–2 years of age because of the deleterious effects of longer periods of right ventricular volume overload.

No age bar for symptomatic ASD cases.

Contraindications

- Irreversible pulmonary hypertension, that is, more than 8–12 units/m^2 at rest or >7 units/m^2 with vasodilators
- Eisenmenger's syndrome

Complications of Surgery

- Atrial flutter/fibrillation, atrial tachycardia and nodal rhythm are seen in the immediate postoperative period.
- Sick sinus syndrome after repair of sinus venosus type of ASD.

ATRIAL SEPTAL DEFECT WITH PULMONARY HYPERTENSION

A marked increase in pulmonary arterial pressure is sometimes found. This, in turn, causes a rise in right ventricular and right atrial pressures. As a result, there is a reversal in the direction of flow through the septal defect and blood is now shunted from the right atrium to the left atrium. Unsaturated blood enters the left atrium and passes to the left ventricle, aorta and systemic circulation. Central cyanosis appears and leads to clubbing of the fingers and polycythaemia.

With the development of pulmonary hypertension, the systolic murmur may disappear and the degree of RVH is increased. The interval between the aortic and pulmonary components of the widely split second heart sound is diminished and the second heart sound becomes closely split. The pulmonary element is accentuated.

The clinical presentation is that of cyanosis and pulmonary hypertension, a combination which may occur in other conditions, for example Eisenmenger's syndrome. The diagnosis of ASD in the presence of pulmonary hypertension may therefore be difficult.

Treatment

Conservative therapy consists of the management of cardiac failure and the prevention and treatment of pulmonary infection. Surgical repair of the defect is now possible under direct vision with the aid of hypothermia or extracorporeal circulation.

PATENT DUCTUS ARTERIOSUS

Patent ductus arteriosus occurs due to the persistence of the communication between the pulmonary artery

and the descending aorta. It is commonly seen in children.

EPIDEMIOLOGY

Incidence: Patent ductus arteriosus constitutes 5%–10% of all congenital heart defects, except in preterm babies where the incidence is slightly more.

Sex: It is more common in females. Female to male ratio is 2–3:1.

EMBRYOLOGY

In foetal life, there is a communication between the left pulmonary artery and the aorta. This is known as ductus arteriosus. It connects the left pulmonary artery, which is just distal, to the bifurcation of the main pulmonary trunk, to the descending aorta. It is distal to the origin of the left subclavian artery, which arises from the left seventh intersegmental artery.

This duct usually closes automatically soon after birth. Oxygen is a potent vasoconstrictor. It plays an important role in closure of the ductus. Non-closure of the duct is known as PDA.

PATHOLOGY

- Term infant with PDA—there is a deficiency of both mucoid endothelial layer and the muscular media of the ductus. Spontaneous closure is rare in this condition.
- Preterm with PDA—the PDA has a normal structural anatomy in preterm babies. The patency may be due to immaturity and hypoxia. Spontaneous closure is possible.

CLOSURE

Normally, the ductus closes after birth. It is larger at the aortic side. The closure of the duct begins from the pulmonary end. In term babies, spontaneous closure is unlikely after 3 months. In preterm babies, spontaneous closure is unlikely after 1 year.

Physiological Closure

Physiological closure (functional closure) begins within a few hours after birth. This is due to the constriction of the muscularis media layer of the ductus. It closes within 14–18 hours. The factors influencing physiological closure are

- rise in PaO_2 and
- reduction of prostaglandin E synthesis due to increased oxygen.

Anatomical Closure

In anatomical closure, the duct is completely sealed by infolding of the ductal epithelium by second to third week after birth. There is proliferation of intima and fibrosis.

Anatomical closure is delayed in preterm children due to defect of elastic tissue in the walls of the ductus. The term baby with PDA may be deficient in mucoid endothelial layer and muscularis media. Hence, the chance of spontaneous closure is less.

Mechanism of Duct Closure

The duct closes by any of the following mechanisms:

- Connective tissue proliferation
- Lumen obstruction—intimal proliferation as well as the disruption and proliferation of subintimal layers cause the sealing of lumen
- Oedema—subendothelial oedema
- Spasm—muscular coil spasm due to local vasoactive amine
- Emboli blocking the ductus
- Endothelium—infolding and ingrowth of endothelium
- Smooth muscle cells—migration of undifferentiated smooth muscle cells

TYPES

The size of PDA depends on the ratio of pulmonary and systemic flow (Q_P:Q_S). Based on these values PDA can be of three types (Table 8.25):

1. Small (<1.5)
2. Moderate (1.5–2.5)
3. Large (>2.5)

This classification helps in planning treatment for the child. Also, it helps in assessing the prognosis

TABLE 8.25 Types of Patent Ductus Arteriosus and Their Differentiating Features

Features	Small	Moderate	Large
Size	<0.5 cm	0.5–1 cm	>1 cm
Left heart overload	Not significant	Moderate	Significant
Murmur	Continuous/systolic	Continuous	Unlikely to be loud or continuous
Pulmonary artery hypertension	Absent	Mild to moderate	Severe
CCF	Absent	±	Present
Timing of surgical closure	12–18 months	6 months–1 year	3–6 months

of the child with PDA. The flow through the shunt depends on the vascular resistance, which is related to the cross-sectional area and the length of the duct. Small PDA can be observed for spontaneous closure or it can be treated medically. Early intervention is indicated for large PDA.

Silent Patent Ductus Arteriosus

This is another type in which there is no murmur. This type is not associated with pulmonary hypertension. It is diagnosed only by ECHO or Doppler. Assisted closure is not recommended in such cases.

HAEMODYNAMICS

The systemic pressure is 120/80 mm Hg. The pulmonary artery pressure is about 25 mm Hg. Hence, there is a flow of blood to the pulmonary artery from the aorta in both systole and diastole. This produces a continuous murmur. The increased pulmonary blood flow leads to pulmonary hypertension. The extent of this left-to-right shunt depends on the following:

- Size of the duct
- PVR
- Degree of prematurity
- Functional capability of the volume-loaded left ventricle

As the pulmonary pressure equals the diastolic pressure, there will be a disappearance of the diastolic component of the continuous murmur. When the pulmonary pressure increases more than the systolic pressure, there will be a reversal of the shunt. This will lead to cyanosis.

The pulmonary hypertension is reversible in the early stages, but later it becomes irreversible. This is a contraindication to the closure of PDA.

PREDISPOSING FACTORS

Patent ductus arteriosus is common in females. The following factors predispose to PDA:

- Gestational age—preterm babies
- Birth weight <1500 g
- Fluid overload due to inadvertent use of intravenous fluids in the newborn period
- Artificial ventilation—ventilator therapy
- Hypoxia/high altitude—oxygen is a stimulus for the closure of PDA. Oxygen levels are low in high altitudes. This is responsible for non-closure of PDA. Isolated PDA is more common in high altitudes
- Congenital infections—rubella
- Drugs—hydantoin, amphetamines
- Exchange transfusion
- Foetal alcohol syndrome
- Intensive phototherapy
- Miscellaneous—anaemia, infections, acidosis and CCF in the newborn period

CONDITIONS ASSOCIATED WITH PDA

The following conditions are associated with PDA:

1. Chromosomal disorders
   - Deletion syndrome—Cri-du-chat syndrome (5p-) and Wolf–Hirschhorn syndrome (4p-)
   - Fragile X syndrome
   - Klinefelter variant (XXXXY)
   - Triploidy

- Trisomy 18
- Trisomy 13
- Pentasomy X

2. Syndromes
   - Carpenter syndrome
   - CHARGE
   - Congenital rubella syndrome
   - Conradi–Hunermann syndrome
   - Crouzon's syndrome
   - Foetal hydantoin syndrome
   - Incontinentia pigmenti
   - Rubinstein–Taybi syndrome
   - Smith–Lemli–Opitz syndrome
   - Treacher–Collins syndrome
   - VATER
3. Maternal conditions
   - Diabetes in the mother—infant of diabetic mother
   - Phenylketonuria
   - Rubella infection
4. Teratogenic agents
   - Amphetamines
   - Hydantoin

CLINICAL FEATURES

1. Child is usually asymptomatic when the ductus is small
2. When the defect is large, in such cases, some or all of the following conditions may be seen:
   - Cardiac failure, with dyspnoea and poor weight gain
   - Frequent chest infections
   - Atelectasis
   - Failure to thrive and growth retardation

Examination of Cardiovascular System

Relevant general examination findings are as follows:

- Pulse—large volume and collapsing
- Bohn's sign—diastolic blood pressure falls during exercise
- Blood pressure—wide pulse pressure. The greater the shunt, the lower will be the diastolic blood pressure

Inspection Findings

- Hyperactive precordium
- Precordial pulsations over the second left ICS

Palpation Findings

Systolic thrill or a continuous thrill is present at the second left ICS. The ductus is situated behind this space. Hence an increased flow in this ductus will cause thrill in this area. Initially the murmur will be continuous. With the development of pulmonary hypertension, the diastolic component will disappear.

Percussion Findings

Dullness is present over the second left ICS due to the presence of the ductus at this site. This is called Gerhard's dullness.

Auscultation Findings

- Continuous murmur, grade IV, best heard in the pulmonary area in the second left ICS in both systole and diastole. This murmur is best heard during expiration. This murmur is also known as machinery murmur, train-in-tunnel murmur, crescendo–decrescendo murmur or Gibson's murmur.
- A middiastolic flow murmur is heard in the mitral area due to increased blood flow across the mitral valve (Fig. 8.22).
- The pulmonary component of the second sound will be loud with the development of pulmonary hypertension.
- As pulmonary hypertension develops, the pressure in the pulmonary artery and the diastolic pressure become equal. At this time there will be disappearance of the diastolic component of the continuous murmur.

SEVERITY

The presence of the following factors indicates that the PDA is severe:

- Wider the pulse pressure, larger is the shunt
- S_3

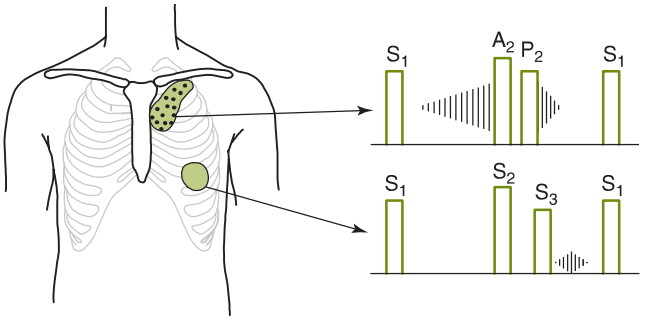


FIGURE 8.22 Auscultatory findings in PDA. Thrill may be present in the dotted area.

- Delayed diastolic murmur
- Cardiomegaly

PATENT DUCTUS ARTERIOSUS WITH PULMONARY HYPERTENSION

A marked increase in the pulmonary artery pressure is sometimes found. It may be due to two factors:

1. Persistence of the foetal pattern of pulmonary arterioles.
2. Reflex vasoconstriction and the development of degenerative changes in the pulmonary arterioles, secondary to the increased pulmonary blood flow.

Patent ductus arteriosus when associated with pulmonary hypertension may have the following effects:

1. Differential cyanosis—the direction of flow through the ductus arteriosus is reversed and blood is shunted from the pulmonary artery to the aorta. Thus, unsaturated blood passes from the pulmonary artery to the aorta. As the ductus arteriosus usually joins the aorta below the origin of the left subclavian artery; unsaturated blood enters the aorta distal to the subclavian artery and passes to the lower limbs. The head and upper limbs are supplied by branches of the aorta proximal to the entry of the ductus arteriosus. They are therefore unaffected by the shunt. Consequently, cyanosis occurs only in the lower limbs and this unequal distribution is known as differential cyanosis.
2. Sometimes, the ductus arteriosus enters the aorta opposite to the left subclavian artery. In these circumstances, unsaturated blood may pass into the left subclavian artery. The left upper limb, therefore, becomes cyanosed in addition to the lower limbs.
3. The continuous murmur disappears. Only a systolic murmur is heard in the pulmonary area.
4. Signs of pulmonary hypertension develop. These are as follows:
   - A diffuse left parasternal impulse due to RVH.
   - An accentuated pulmonary element of the second heart sound.
   - Electrocardiographic evidence of RVH and strain.
   - Enlargement of the right ventricle on radiological examination.

DIFFERENTIAL DIAGNOSIS

Continuous murmur will be heard in the following conditions:

- Aortopulmonary window—murmur best heard in the left third ICS
- Bronchopulmonary collaterals in TOF, coarctation of aorta. Murmur is present bilaterally in the ICSs
- Coronary arteriovenous fistula—murmur at the apex
- Rupture of sinus of Valsalva—sudden onset with CCF

- Peripheral pulmonary artery stenosis—murmur is superficial; it is not localised and can be heard all over the thorax
- Systemic arteriovenous fistula—associated with a bounding pulse
- Pulmonary arteriovenous fistula—associated with cyanosis and clubbing. Angiogram confirms the diagnosis
- Venous hum—varies with posture
- Persistent truncus arteriosus—usually associated with cyanosis
- Absence of pulmonary valve—'to and fro' murmur
- TAPVD into the right atrium. The murmur is similar to venous hum

Combination of pansystolic murmur and regurgitant diastolic murmur.

- VSD with AR—the murmur is maximally audible at the left lower sternal border. The character of the murmur in VSD with AR will be 'to and fro' then 'continuous.'
- Mitral regurgitation with atrial regurgitation.

INVESTIGATIONS

1. ECG—it is suggestive of left ventricular enlargement (due to volume overload) and RVH (due to pressure overload)
   (a) Small PDA—in mild cases the ECG is normal.
   (b) Moderate PDA
      - Left atrial enlargement
      - Left ventricular enlargement due to volume overload
   (c) Large PDA
      - When the shunt is large, there is LVH. Tall 'R' in left ventricular leads, usually in V_5 and V_6 leads. Deep S waves in right ventricular leads, usually in leads V_1 and V_2. In addition, left ventricular strain may occur as shown by inversion of T waves and depression of 'ST' segments in left ventricular leads
      - Biventricular hypertrophy
2. Chest X-ray (Fig. 8.23)
   (a) Cardiomegaly—enlargement of the left ventricle

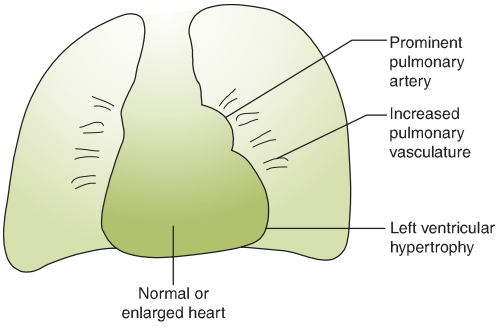


FIGURE 8.23 Radiological findings in PDA.

   (b) Increased vascularity of the lung fields—plethoric lung fields
   (c) Aortic knob normal or prominent
   (d) Prominence of the pulmonary conus
   (e) Dilatation of the pulmonary artery and its branches
   (f) Enlargement of the supracardiac 'aortic' shadow. The space between the pulmonary artery and the aortic knuckle is obliterated by the PDA
   (g) Hilar dance on fluoroscopy—conspicuous pulsation of the pulmonary arteries is known as hilar dance on fluoroscopy. The pulsations, however, are not as marked as in ASD
3. ECHO—the patent duct is better viewed through suprasternal approach or parasternal short axis view.
4. Doppler study—helps to view the direction and amount of flow in the ductus.
5. Cardiac catheterisation
   (a) Visualisation of the catheter—the catheter is often seen to pass through the ductus arteriosus into the aorta
   (b) Oxygen studies—samples of blood taken from the pulmonary arteries, especially the left, show a higher percentage of oxygen saturation than samples from the right ventricle, right atrium and SVC
   (c) Pressure studies—the pressure in the pulmonary artery is normal in mild cases and moderately raised when the shunt is large
6. Angiocardiography
   (a) This is occasionally performed when the

diagnosis is in doubt

(b) The best method for demonstrating the ductus is retrograde aortography. A catheter is passed through a peripheral artery into the arch of the aorta and dye is injected

TREATMENT

Ideal Age for Intervention

- Small PDA—wait and follow-up for spontaneous closure.
- Moderate PDA—wait up to 2 years or until the baby weighs 10 kg.
- Patent ductus arteriosus with symptoms such as CCF and infective endocarditis—close the PDA surgically.

Medical

1. Treatment to close the PDA—it is advised when the PDA is seen in a preterm child and when the PDA is likely to close spontaneously
   (a) Indomethacin—closure of the PDA occurs by giving indomethacin in a dose of 0.1–0.2 mg/kg at 12 hourly intervals for three doses. This is most effective in preterm babies. The ductus in a term baby is not sensitive to prostaglandin, so this is not used in term babies. Ideally, it is given within 48–72 hours after birth. Indomethacin acts by reducing prostaglandin E (PGE) levels. Before giving indomethacin, investigate for neutropenia, renal function and neonatal necrotising enterocolitis (NNEC). The following are the contraindications:
      - Anuria/oliguria
      - Bilirubin increased (hyperbilirubinaemia)
      - Bleeding tendency
      - Blood urea nitrogen >25 mg/dL
      - Creatinine levels >1–8 mg/dL
      - Decreased platelet count <50,000/mm^3
      - Enterocolitis—NNEC

   (b) Ibuprofen—it is tried in babies with renal problems, where indomethacin is contraindicated

TABLE 8.26 Modes of Treatment Depending on the Age

Age (months)	Modes of Treatment
<6	Surgical closure
>6	Occlusive devices Coil occlusion Surgical closure

2. Treatment of associated conditions
   (a) Cardiac failure (see section *Congestive Cardiac Failure*, page 376)
      - Avoid fluid overload—fluid restriction.
      - Diuretics.
      - Digoxin—the dose of digoxin should be decreased in preterm babies less than 32 weeks of gestation.

If PDA does not close spontaneously or by medical management, interventional procedures or surgical closure can be opted based on the age of the child (Table 8.26).

Interventional Procedure

It involves non-surgical closure using an umbrella device. Transcatheter closure of PDA is done with a Teflon plug or intravascular coils. The following devices can be used:

- Rashkind occluder—double umbrella occlusion system
- Spring coils—for PDA up to 2.5–3 mm
- Amplatzer PDA occluder—for ducts larger than 2.5 mm. It is a self-expanding mushroom-shaped device made of nitinol wire mesh. The PDA is closed by induction of thrombogenesis, which is accomplished by the polyester fibre sewn securely into the device
- Sideris device

Indications for closure of PDA by interventional procedures are as follows:

- Term baby
- Failure of medical treatment
- PDA with cardiac failure

Optimal age for intervention is during the first year of life. In the absence of symptoms, the procedure can be delayed until 6 months. The contraindications are as follows:

- High pulmonary artery pressure/POVD
- Eisenmenger's syndrome

Surgical Closure

It is done by double ligation of PDA. As the ductus is friable, division may be avoided. Postsurgical mortality is less than 1%.

OBLIGATORY PATENT DUCTUS ARTERIOSUS

In certain conditions such as hypoplastic left heart syndrome and transposition of great vessels, the presence of patent ductus is essential for existence of life. In the absence of the blood flow in the ductus, the child will die. This is called an obligatory PDA. The conditions that require a patent ductus are as follows:

1. Ductus is the only means of the pulmonary blood flow
   - Pulmonary atresia with intact ventricular septum
   - Tricuspid atresia with intact septum
2. Ductus is the only means of the systemic blood flow
   - Aortic atresia
   - Preductal coarctation of aorta
   - Hypoplastic left heart syndrome
3. Ductus is the means of bidirectional blood flow—transposition of great arteries with intact septum

Maintenance of a Patent Ductus Arteriosus

A continuous infusion of PGE is needed for the maintenance of a patent ductus. Prostaglandin infusion at 0.01–0.1 µg/kg/minute will ensure ductal patency in duct-dependent conditions. The prostaglandin E_1 (PGE1) infusion in a dose of 0.01 µg/kg/minute is given. This can be given by the following preparation; 30 µg of prostaglandin is added to 50 mL of normal saline and infused at a rate of 1 mL/hour. Side effects of this infusion are hypotension and apnoea. This drug is usually given for 2–3 days, up to a maximum of 7 days. Surgery should be planned during this time.

BOX 8.2 Mnemonics for complications of patent ductus arteriosus

A	Aneurysms of the duct or pulmonary artery
B	Blockage of arteries due to pulmonary and systemic embolism/paradoxical embolism or thrombosis
C	Calcification of the ductus
D	Ductal endarteritis
E	Eisenmenger's syndrome
F	Failure—congestive cardiac failure
G	Growth retardation
H	(Pulmonary) hypertension
I	(Recurrent respiratory) infections

COMPLICATIONS

- Congestive cardiac failure
- Pulmonary hypertension
- Eisenmenger's syndrome
- Recurrent respiratory infections
- Ductal endarteritis
- Aneurysms of the duct
- Paradoxical embolism
- Growth retardation
- Calcification of the ductus
- Pulmonary and systemic embolism

These are summarised in Box 8.2.

PROGNOSIS

Spontaneous closure of the ductus after the infancy is rare. The prognosis of the PDA in preterm babies is good. The PDA in preterm babies usually closes spontaneously in the early infancy. There may be a defect in the elastic tissue of the duct in preterm babies.

The PDA that occurs in term babies is usually due to some defect in the duct, therefore it does not close spontaneously. The infant can be observed for 3 months. If there is no spontaneous closure, surgical intervention should be done to close the PDA.

TETRALOGY OF FALLOT

It is a cyanotic heart disease that occurs in more than 10% cases of all congenital heart diseases. Males are more often involved.

COMPONENTS

1. Pulmonary infundibular stenosis (pure valvular stenosis/combination of valvular and infundibular stenosis also occurs).
2. High VSD—the septal defect is situated in the membranous or subaortic part of the interventricular septum.
3. Overriding of aorta—the overriding aorta is due to an abnormality of the aortic root. The aorta is not in alignment with the left ventricular outflow tract but is displaced to the right (dextroposed) and overlies or 'over-rides' the interventricular septum from which it is separated by the high septal defect.
4. Right ventricular hypertrophy (concentric) is not a developmental abnormality but is due to the altered haemodynamics caused by the above three malformations.

Only two abnormalities are actually required—a VSD large enough to equalise the pressures in both the ventricles and a right ventricular outflow obstruction. The RVH is secondary to the right ventricular outflow obstruction. Overriding of aorta is not a requirement (Fig. 8.24).

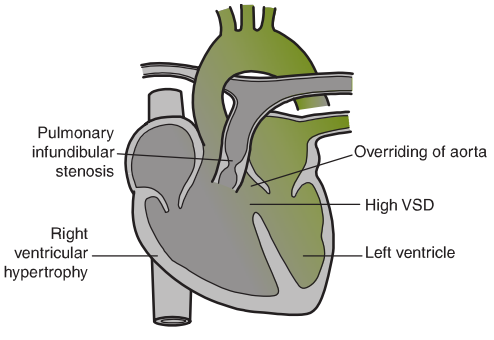


FIGURE 8.24 Tetralogy of Fallot.

EMBRYOLOGY

- Anterocephalad malalignment of the infundibular (outlet) septum with the muscular (trabecular) septum is the hallmark of TOF. This is the cause of right ventricular outflow tract obstruction, overriding of aorta and a high VSD.
- Arrested development of the bulbus cordis results in malformation of the root of the pulmonary artery and its valves leading to infundibular or valvular stenosis.
- Incomplete rotation of the spiral septum is responsible for dextroposition and overriding of aorta.
- Failure of the aortic septum to meet the interventricular septum inevitably results in a high interventricular septal defect.

ASSOCIATED DEFECTS

- Right-sided aortic arch in 25% of cases
- Anomalous distribution of coronary arteries in 2%–10% of cases
- Atrial septal defect in 15% of cases
- PDA
- Persistent foetal circulation
- Absence of left pulmonary artery
- Pulmonic valve is frequently absent or bicuspid
- Hypoplastic pulmonary trunk and its branches
- The lungs are perfused by systemic collaterals or by PDA in severe cases
- Persistent left SVC

COMPENSATORY MECHANISMS

- Polycythaemia—this alleviates the anoxaemia but may aggravate the cyanosis (Fig. 8.25).
- Development of an extensive collateral circulation between the branches of the aorta and the pulmonary arteries—the principal vessels involved are the bronchial arteries, which originate from the descending portion of thoracic aorta. Less important collateral channels develop from mediastinal, oesophageal and internal mammary and pericardial arteries. This collateral circulation enables part of the mixed saturated



FIGURE 8.25 Polycythaemia with cyanosis in a case of TOF.

and unsaturated blood in the aorta to reach the lungs for oxygenation.

- Persistent PDA—tetralogy of Fallot with absence of pulmonary oligaemia may be due to persistence of PDA (delayed closure of the ductus arteriosus). In Fallot's tetralogy, the ductus arteriosus forms an important channel enabling blood to be shunted from the aorta to the pulmonary artery and then to the lungs for oxygenation. This compensatory mechanism is only temporary, as the ductus arteriosus eventually undergoes obliteration. Closure, however, is delayed often up to 1 year.

CONDITIONS ASSOCIATED WITH TOF

- Chromosomal anomalies—deletion syndrome (l0 q-), Down's syndrome, trisomy 18 (Edward's syndrome), etc.
- Syndromes—Goldenhar syndrome, VATER syndrome, DiGeorge syndrome, Laurence–Moon–Biedel syndrome, CHARGE syndrome, velocardiofacial syndrome, TAR syndrome, Poland syndrome, Cornelia–Delange syndrome, Alagille syndrome, foetal alcohol syndrome, foetal hydantoin syndrome.
- Maternal conditions—phenylketonuria in mother may predispose to TOF.
- Teratogenic agents—drugs that may cause TOF are thalidomide, trimethadione, carbamazepine, sex hormones and so on.

HAEMODYNAMICS

The pressures in both the ventricles are equal because of the large VSD. In addition to the VSD there is a PS. This leads to partial ejection of the right ventricular output into the pulmonary artery and remaining to the aorta through the VSD. This deoxygenated blood, which enters the systemic circulation, mixes with the oxygenated blood from the left ventricle and leads to cyanosis.

Acyanotic Fallot

In this condition the obstruction to the pulmonary flow is minimal. So, the blood flow to the pulmonary artery is good and enough blood gets oxygenated to prevent cyanosis. Thus even in the presence of the defects, the child is pink (not cyanosed), hence it is also know as pink Fallot.

Cyanotic Fallot

In this condition the pulmonary resistance is high and the blood flow to the pulmonary circulation is decreased. There is an increased shunting of blood from right to left side aggravating the central cyanosis.

The flow from right ventricle to the stenosed pulmonary artery produces an ESM. The severe the PS, the shorter is the ESM, and more the cyanosis. The intensity of the ESM is inversely proportional to the severity of PS.

CLINICAL FEATURES

- Growth retardation
- Central cyanosis (cyanosis may be missed, if it is mild)
- Clubbing
- Chest pain due to hypoxia
- Headache due to hypoxia
- Tachypnoea
- Dyspnoea/breathlessness—the degree of exertional dyspnoea varies with the severity of the anatomical defects
- Syncope—common in infancy and may be precipitated by exertion. It is a common cause of death in infancy

Cyanotic Spells

Also known as hypoxic spells or tet spells, occur in young infants, more common between 2 and 4 months of age. They are the result of an abrupt reduction in pulmonary blood flow or a decrease in systemic vascular resistance (SVR). Characteristic features are as follows:

- Paroxysm of hyperpnoea (rapid and deep breathing)
- Sudden marked increase in cyanosis
- Irritability and prolonged crying
- Decreased intensity of the heart murmur

There may be limpness or convulsions, and occasionally death.

Precipitating Factors

Exercise, sedation, fever and general anaesthesia decrease the SVR and increase the right-to-left shunt flow causing cyanosis. The spells usually occur in the morning, following defecation, crying or feeding. Supraventricular tachycardia provokes the spell.

Pathophysiology

The right ventricle and left ventricle can be considered as a single pumping chamber, since there is a large VSD equalising pressures in both ventricles. Lowering of the SVR or increasing resistance at the right ventricular outflow tract increases the right-to-left shunt. The resulting decrease in arterial oxygen saturation stimulates the respiratory centre to produce hyperpnoea. Hyperpnoea results in a further increase in systemic venous return, which, in turn, increases the right-to-left shunt through the VSD, because of the presence of PS. A vicious cycle is then established (Fig. 8.26).

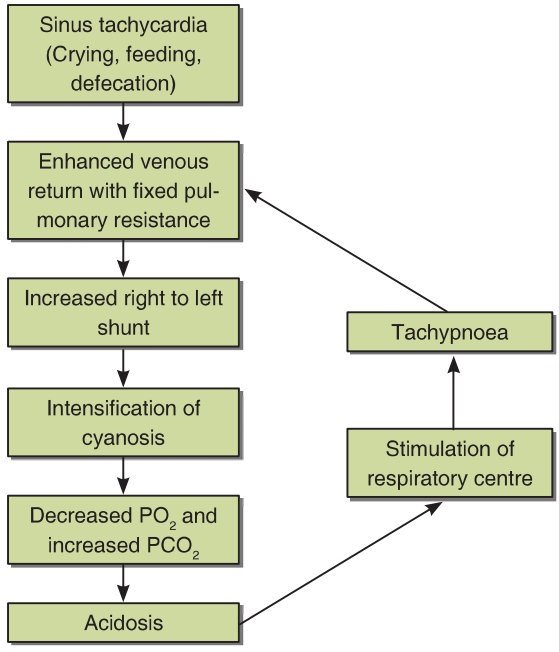


FIGURE 8.26 Mechanism of hypoxic spell.

Postural Adaptation

A special posture is adopted by children with right-to-left shunts to increase arterial oxygen saturation. Adoption of these postures helps in breaking the vicious cycle in hypoxic spells by temporarily trapping the desaturated blood in lower limbs. These are as follows:

1. Squatting
2. Squatting equivalents
   - Knee–chest position
   - Sitting with legs drawn underneath
   - Cross the leg when standing
   - Lying down
   - Sitting on the chair with flexed legs
   - Baby sitting on the mother's hip with legs flexed

Mechanism. Squatting or its equivalents helps in decreasing the cyanosis in the following ways:

- Increases the SVR (by reducing the blood flow in femoral arteries), thereby increasing the pressure by which the right ventricle contracts. This increased force of contraction overcomes the pulmonary resistance to a certain extent and the pulmonary flow increases. This also reduces the venous washout from the muscles with low saturation.
- Decreases the venous return from the legs. This decreases the inflow of highly unsaturated blood; this also helps in decreasing the degree of cyanosis. Arterial oxygen saturation will be improved and arterial lactate decreased as a result of decreased venous return from the active leg muscles.
- Increases the intrathoracic pressure, thereby helping in decreasing the venous return.

Central Cyanosis

The usual age of onset of cyanosis depends on the severity of right ventricular outflow obstruction.

1. Severe degree of right ventricular obstruction can present with cyanosis at birth or in the newborn period.
2. Mild degree of right ventricular obstruction can present with cyanosis anytime after birth but usually by 6–12 months of age. The factors responsible for this late onset of cyanosis are as follows:
   - Foetal haemoglobin prevents the cyanosis. The foetal haemoglobin has high affinity for oxygen.
   - Activity of the child is more after 6 months as the child begins its playful activities and therefore oxygen demand is more. This aggravates the cyanosis.
   - Patent ductus arteriosus may be patent and the flow in it may compensate for the decreased pulmonary flow.
   - Emotional development—the child develops a period of negativism by 6–7 months of life. These emotions cause spasm of the smooth muscles.
   - Pulmonary infundibular muscular development occurs with the growth of the child. This leads to an increased obstruction to the pulmonary flow from the right ventricle.

Examination Findings

1. Pulse and blood pressure are normal. Blood pressure may be increased in the later stages, after several years of marked cyanosis and polycythaemia.
2. Cyanosis and clubbing may be present.
3. Heart sounds (Fig. 8.27)
   - First heart sound is normal.
   - S_2 is usually single; only the aortic component is heard. Since the aorta is placed anteriorly, this is loud.
   - P_2 is delayed and soft; it is inaudible. This is due to decreased blood flow and associated PS.
   - Sometimes, an aortic ejection click may be heard. A constant ejection click may be heard due to large aorta. An inconstant ejection click may be heard due to valvular PS.
4. Murmurs—ejection systolic murmur is heard in the left third and fourth ICSs due to flow from right ventricle to stenosed pulmonary artery. The intensity and duration of the murmur is inversely proportional to the pulmonary artery obstruction.

NATURAL HISTORY

Children with the acyanotic form of TOF gradually develop cyanosis by 1–3 years of age. Symptoms

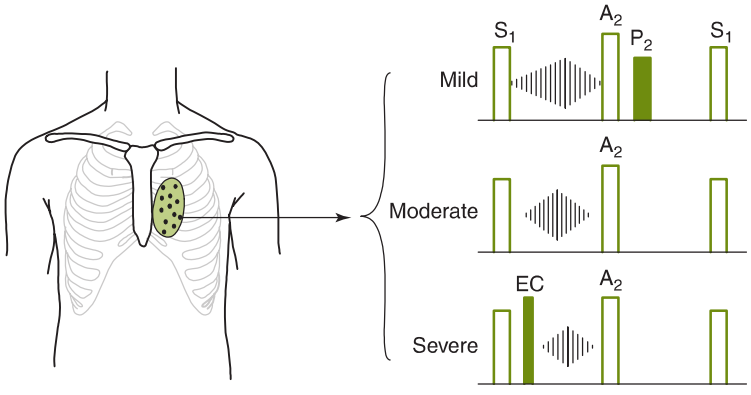


FIGURE 8.27 Auscultatory findings in TOF. Thrill may be present in the dotted area.

tend to progress because of increasing severity of the infundibular stenosis.

Infants, who develop cyanosis in the first month of life, usually have severe PS. These infants have symptoms such as marked dyspnoea and exercise intolerance. If these patients survive, they improve after the first or second year of life, possibly due to the development of collaterals.

DIFFERENTIAL DIAGNOSIS

- TGA with pulmonary stenosis
- Double outlet right ventricle with pulmonary stenosis with VSD
- Single ventricle with pulmonary stenosis
- VSD with pulmonary stenosis
- TGA with VSD with pulmonary stenosis
- VSD with pulmonary atresia
- Tricuspid atresia
- Truncus arteriosus—type IV
- Eisenmenger's syndrome/Eisenmenger's complex
- Isolated pulmonic stenosis, with intact aortic root with right-to-left shunt through patent foramen ovale.

INVESTIGATIONS

1. ECG
   - Right axis deviation
   - Right ventricular hypertrophy
2. X-ray
   - Normal-sized heart/small heart
   - Conspicuously clear lung fields due to pulmonary oligaemia
   - Boot-shaped heart (Coeur en sabot)—the concavity is due to pulmonary oligaemia, underdeveloped main pulmonary artery. The apex is elevated due to the RVH (Fig. 8.28). Right-sided aortic arch in 30% of the patients
   - Right ventricular enlargement (lateral view)
   - Hypertrophy of the right ventricle displacing the left ventricle upwards and to the left, thereby producing the appearance of a wooden shoe with an upturned toe—the 'Coeur en sabot.

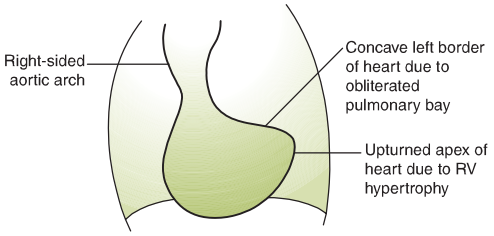


FIGURE 8.28 Boot-shaped heart in TOF.

   - A distinct concavity between the aortic knuckle and the ventricle due to hypoplasia of the pulmonary artery
3. Echocardiogram shows the infundibular stenosis, high VSD and RVH
4. Colour Doppler study will show the flow of blood from the right ventricle into the aorta
5. Selective right ventriculography
   - Simultaneous opacification of the pulmonary artery and aorta
   - The flow from right ventricle to the aorta directly can be seen
   - Boot-shaped heart
   - Right-sided aortic arch in 30% of the patients
   - Right ventricular enlargement (lateral view)
6. Left ventriculography
7. Aortography
8. Coronary arteriography—in 50% of cases with TOF, an aberrant coronary artery crosses over the right ventricular outflow tract
9. CT scan—for brain abscess
10. MRI—for brain abscess
11. Cardiac catheterisation—right heart catheterisation is useful to differentiate TOF from PS, with normal aortic arch. The catheter is passed into the overriding aorta from the right ventricle
    - Visualisation of the catheter—the catheter may be passed through the interventricular septal defect and visualised in the aorta or left ventricle
    - Oxygen studies—samples of blood from a systemic artery, for example, femoral artery, show decreased oxygen saturation. The oxygen saturation of samples from the vena

cava, right atrium, right ventricle and pulmonary artery is proportionately diminished and well below the normal venous percentage oxygen saturation range of 70%–80%

- Pressure studies—the pressure in the pulmonary artery is low; the pressure in the right ventricle is greatly increased and approximates that in the left ventricle

TREATMENT

Medical

1. Treatment of cyanotic spell—aim of treatment is to break the vicious circle by the following methods:
   - Holding the infant in knee–chest position traps venous blood in legs and decreases the systemic venous return.
   - Oxygen administration improves arterial oxygen saturation.
   - Morphine is anxiolytic and depresses the respiratory centre. It also acts as a dilator of venous capacitance, there by decreasing the venous return. Paraoxysmal hyperpnoea will respond dramatically to morphine in relatively large doses (0.2 mg/kg body weight).
   - Intravenous propranolol (0.1 mg/kg) relives the subpulmonary muscular spasm, which is the cause of reduced pulmonary blood flow. It also acts as a peripheral vasoconstrictor and increases systemic venous resistance.
   - Vasoconstrictors, such as phenylephrine 0.02 mg/kg intravenously, raise the SVR and force more blood to the lungs.
   - Treatment of acidosis—sodium bicarbonate 2 mL/kg (1 mEq/kg) is given intravenously to abolish acidosis and its stimulating effect on the respiratory centre.
   - Muscle paralysis and artificial ventilation in order to reduce the metabolic oxygen demand.
2. Treatment of polycythaemia—phlebotomy and volume replacement with fresh frozen plasma.
3. Maintenance of a patent ductus—prostaglandin E_1 in a dose of 0.05–0.20 μg/kg/minute causes dilatation of ductus arteriosus and provides adequate pulmonary flow until surgical repair is done.
4. Prevention of complications—the following preventive measures should be taken to prevent complications:
   - Avoid dehydration—due to the presence of polycythaemia, any factor that diminishes the available plasma volume is dangerous.
   - Relative iron deficiency anaemia (IDA) is treated with iron. The diet for children with TOF should have more iron. Folic acid supplementation is also required due to increased production of red blood cells (RBCs).
   - Prophylaxis against infective endocarditis—antibiotic cover for infections, surgical and dental procedures and maintenance of good oral hygiene.
   - Oral propranolol therapy may prevent the cyanotic spells.
   - Precautions to avoid clot formation during intravenous infusion are needed. Any clot in the circulation will predispose to paradoxical embolism.

Surgical

Timing of Surgery

- Surgery is done at birth or later in infancy depending on the severity of defects, weight and general health of the baby, and severity of the symptoms.
- When severe symptoms develop in the first or second month of life, an initial shunting operation should be done which is followed by repair within 12 months.
- When a patient is asymptomatic or only mildly symptomatic, repair can be deferred until 2 years of life.
- In severe TOF, surgery can be done in neonatal period.
- In babies who are too small or too weak, palliative surgery can be done immediately and total corrective elective surgery can be done in late infancy.

Palliative Shunt Procedures

Indications

- Recurrent spells
- Packed cell volume >65
- Children who can not tolerate total correction
- Anatomical abnormality—not good for correction; extremely small pulmonary artery is one such condition
- Infants who become symptomatic in the first few months of life

Types of Palliative Surgery. A total correction cannot be done immediately after the diagnosis because the size of the pulmonary artery is small due to decreased flow. So, it is better that the size of the pulmonary artery be increased by increasing the pulmonary blood flow by certain procedures as given below (Fig 8.29):

1. *Blalock–Taussig shunt* (subclavian and pulmonary artery anastomosis)—subclavian artery is shunted to the ipsilateral pulmonary artery. In patients with right-sided aortic arch, left subclavian artery is shunted to the left pulmonary artery and in patients with left-sided aortic arch, right subclavian is shunted to the right pulmonary artery.

   This procedure will result in absent radial pulse on the side of the shunt and a continuous murmur at the level of shunt.
2. *Modified Blalock–Taussig shunt*—subclavian artery is shunted to the ipsilateral pulmonary artery, using a conduit. Gore-Tex interposition shunt between the subclavian and the ipsilateral pulmonary artery is the procedure of the choice in small infants younger than 3 months. A left-sided shunt is performed in patients with left aortic arch, and a right-sided shunt in patients with right-sided aortic arch.
3. *Waterston shunt* (ascending aorta to right pulmonary artery anastomosis)—it is not performed because of complications such as large shunt (CHF, pulmonary hypertension), narrowing and kinking of the right pulmonary artery at the site of anastomosis.
4. *Potts–Smith shunt*—rarely performed because of complications such as CCF and pulmonary hypertension. It consists of direct side-to-side anastomosis of the descending aorta to the left pulmonary artery. In modified Potts operation, a graft is put between the aorta and pulmonary artery. The advantage of this procedure is that the aortic pressure does not directly go to the pulmonary artery.
5. *Glenn's shunt*—superior vena cava is anastomosed to the right pulmonary artery.
6. *Barret's procedure*—a palliative procedure. Stripping of pleura on both sides will lead to formation of granulation tissue. This predisposes to formation of collaterals, which increases the pulmonary flow. Collaterals develop from the following vessels:
   - Aorta
   - Intercostal arteries
   - Internal mammary arteries
   - Bronchial arteries

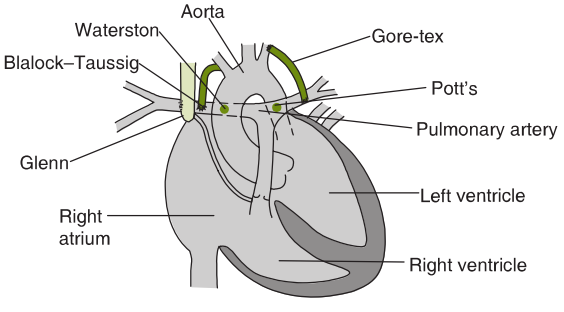


FIGURE 8.29 Types of palliative surgery in TOF.

Total Correction

It is the definitive treatment. If the pulmonary artery is good, surgery can be done at any age. Left atrium to aortic root ratio should be 1:1 (at least 0.8) for total correction.

Types of total correction are as follows:

- *Brock's procedure* (transventricular valvotomy or infundibulectomy)—the infundibulum is resected and the patch closure of VSD is done. Pulmonary valvotomy may also be done. Removing the obstruction to the pulmonary artery blood flow in the presence of a large VSD will predispose to pulmonary congestion and ultimately pulmonary vascular obstruction.
- *Rastelli's operation*—it is done for cases with severe hypoplasia or atresia of the right ventricular outflow

tract. This is usually done after 5 years of age. The pulmonary artery is divided from the left ventricle and the cardiac end is overseen. An intracardiac tunnel is placed between the large VSD and the aorta so that the left ventricle communicates with the aorta. The right ventricle is connected to the divided pulmonary artery by an aortic homograft or a valve bearing prosthetic conduit.

Complications of Surgery

Surgery can result in complications such as CCF, bleeding problems, pulmonary valve regurgitation, RBBB, complete heart block, ventricular arrhythmias, incomplete closure of VSD, diaphragmatic paralysis and Horner's syndrome.

CONSEQUENCES AND COMPLICATIONS

- Anaemia
- Polycythaemia (secondary to hypoxia)
- Cyanotic spells
- Growth retardation—failure to thrive
- Pressure on the trachea by enlarged aorta (stridor and wheezing)
- Disseminated intravascular coagulation (DIC)
- Bleeding disorders—thrombocytopenia, defective platelet aggregation, prolonged PT, aPTT, decreased levels of factor V and VIII. These manifests as easy bruising, epistaxis and gum bleeds
- Haemoptysis may be due to disseminated intravascular coagulation, bronchopulmonary collaterals, thrombocytopenia or polycythaemia
- Arthritis
- CNS complications—brain infarction (common below 2 years of age) and brain abscess (common after 2 years of age). The abscess resulting from haematogenous spread commonly occurs at the junction of white and grey matter, the area which is rich in blood supply. Histologically there are four stages of abscess formation, namely early cerebritis (day 1–3), late cerebritis (day 4–9), early encapsulations (day 10–13) and late encapsulations (day 14 onwards). The capsule is poorly formed on the medial side (ventricular side) due to poor blood supply. The abscess may rupture into the ventricles. The organisms causing brain abscess are Peptostreptococcus, Bacteroides and Streptococcus which are commonly see in the oral cavity
- Gout and hyperuricaemia due to increased destruction of RBCs
- Infections—pulmonary tuberculosis (common)
- Paradoxical emboli/thromboembolic manifestations such as thrombosis of cerebral veins/sinuses within the duramater
- Metabolic acidosis due to prolonged anaerobic metabolism
- Psychosocial limitations

CONGESTIVE HEART FAILURE AND TOF

Congestive heart failure is rarely seen since the right ventricle is decompressed effectively by the VSD. Congestive cardiac failure does not occur in TOF. Rarely, CCF occurs in the presence of the following conditions:

- Anaemia
- Infective endocarditis
- Systemic hypertension
- Myocarditis
- Presence of collaterals—bronchopulmonary collaterals
- After Blalock–Taussig shunt.
- Other associated cardiac defects such as PDA and AR
- Pink Fallot

VARIANTS

There are two variants of TOF.

1. *Trilogy of Fallot*—it consists of ASD, PS and right ventricular hypertrophy.
2. *Pentalogy of Fallot*—components of TOF associated with patent foramen ovale or ASD.

RHEUMATIC FEVER

Rheumatic fever is an immunological disorder that follows infection of the pharynx by group A beta-haemolytic streptococci. It affects the heart, joints, CNS, skin and subcutaneous tissue. It is a non-infectious,

non-suppurative sequelae of streptococcal pharyngitis and occurs 10 days to several weeks after the attack of sore throat.

EPIDEMIOLOGY

Age group: 5–15 years.

Gender: Incidence of rheumatic disease is equal in males and females. Mitral valve disease and chorea are common in females, and aortic valve involvement is common in males.

Prevalence in India: 0.6 /1000.

Attack rate of rheumatic fever after streptococcal pharyngitis is 3% in children who are not treated or inadequately treated.

AETIOLOGY

- Group A β-haemolytic streptococcus—pathogenic strains are M type, 1, 3, 5, 6, 18, 19, 24. Type 18 is the most virulent mucoid strain.
- Viral—not proved yet.
- Genetic influence—the presence of a specific alloantigen on the surface of non-T lymphocytes in 70%–90% of rheumatic fever patients (inherited as Mendelian recessive pattern) favours genetic predisposition.
- Autoimmunity.

PATHOGENESIS

There are three proposed hypothesis by which it affects the human system:

1. Direct infection of the heart valves by group A beta-haemolytic streptococci. Since the streptococci have not been isolated from the lesions in the heart and joints, this hypothesis is not proven.
2. Extracellular toxin produced by the streptococci affecting the myocardium, valves, synovium and brain; again this is not proved.
3. An abnormal immune response generated by the individual in response to infection. This has also been not proved, but the latent period of 1–3 weeks between the onset of sore throat and the rheumatic fever supports this theory.

Immune Response to Streptococci

There is cross-reactivity between the streptococcal cell wall proteins as well as carbohydrates and the human connective tissue. In other words, the antibodies produced by the streptococcus cross-react with the human tissue. Group-specific polysaccharide *N*-acetyl glucosamine of streptococcus is antigenically similar to glycoproteins found in human cardiac valves. This initiates an abnormal autoimmune response against sarcolemmal membrane of the myocardium. Cross-reactivity is also present between the streptococcal 'M' protein and the human tissue.

PATHOLOGY

- The inflammatory lesion is present in the heart, joints, brain and skin.
- Aschoff body in the atrial myocardium is the most characteristic feature of rheumatic fever. It is present only in acute stage and undergoes progressive fibrosis.
- Mitral valve is the commonest valve to be affected followed by the aortic and tricuspid valves in that order. Pulmonary valves are almost never affected in cases of RHD.
- The valves on the left side are commonly involved due to the greater strain on these valves. Initially, there is MR which is later followed by fibrosis of the valve leading to MS. Diffuse thickening of the valves may occur.
- Rheumatic vegetations are small beaded vegetations, such as warty nodules, present on the margins of the valves. The verrucae are seen along the line of closure of the valves where the leaflets impinge on each other. The surface of the valve exposed to the forward flow is affected. There is adherence of leaflets at the commissures. The verrucae may also be seen in the chordae tendinae. Rheumatic vegetations are formed due to aggregation of platelet thrombi, which get deposited in the endothelium. McCallum's patch is seen on the posterior wall of the left atrium above the mitral valve. Often this forms a nidus for infective endocarditis. There is oedema and swelling of valves, formation of new vessels and later fibroblastic proliferation. The valvulitis may resolve without any deformity or may undergo

fibrous scarring resulting in deformity. This is a chronic process and results in the vegetation of the valves becoming fibrous and blending together with thickened cusps. The chordae tendinae may also get affected and lead to shortening of the chordae.

RISK FACTORS

The risk factors for rheumatic disease are as follows:

- Upper respiratory tract infection (streptococcal)
- Poor socioeconomic class—overcrowding, poor nutrition and unhygienic surroundings
- Seasonal variation—high incidence in fall, winter and early spring months
- Climate—temperate subtropical and tropical
- Epidemics of streptococcal throat infection (highly virulent organisms and poor resistance to infections)
- Hereditary predisposition—rheumatic fever tends to run in families, which indicates that there may be a genetic predisposition. HLA association is seen. It is seven times more common in instances of monozygotic twins as compared to instances of dizygotic twins
- Previous attack carries a risk of 50% recurrence

CLINICAL FEATURES

It is commonly said that rheumatic disease 'bites the heart, licks the joint and kicks the brain.'

- Symptoms occur about 1–5 weeks (average 2–3 weeks) after an initial attack of pharyngitis. History of preceding sore throat is present in 50% people.
- Fever, anorexia, lethargy and joint pains may be present.
- Family history of rheumatic fever is often positive.

Revised Duckett Jone's Criteria

This criterion is commonly used in diagnosing rheumatic disease. It is further divided into major, minor and essential criteria (Table 8.27) as follows:

TABLE 8.27 Revised Jones Criteria for Rheumatic Fever

Major	Minor	Essential Criteria
Carditis[a] Arthritis[a] Subcutaneous nodules Chorea Erythema marginatum	Clinical • Fever • Arthralgia Laboratory • Increased ESR, CRP • Prolonged P-R interval	Evidence of antecedent streptococcal infection

[a]In presence of arthritis, arthralgia is not taken as minor criteria, and in presence of carditis, prolonged P-R interval is not taken as minor criteria.

1. Major criteria (more specific)
   (a) Carditis
   (b) Arthritis
   (c) Subcutaneous nodules
   (d) Chorea (Sydenham's chorea, St. Vitus dance)
   (e) Erythema marginatum
2. Minor criteria (less specific)
   (a) Clinical
      - Fever
      - Arthralgia

   (b) Laboratory
      - Elevated acute phase reactants—erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)
      - Prolonged P-R interval—prolongation of P-R interval is the earliest sign of conduction blocks. Normal P-R interval varies with age as given in Table 8.28
3. Essential criteria—this refers to supporting evidence of antecedent streptococcal infection
   (a) Increased or rising antistreptolysin O (ASO) titer—the normal values are usually below 160 Todd units per milliliter. However, only values above 333 Todd units are significant

TABLE 8.28 Normal P-R Interval in Various Age Groups

Age Group (years)	*P-R* Interval (seconds)
3–12	0.16
12–14	0.18
>17	0.20

TABLE 8.29 Significant Levels of ASO Titer in Children and Adults

Age Group	Significant Levels (Todd units per millilitre)
Children 5–15 years	>333
Adults	>250

TABLE 8.30 Normal Levels of Anti-DNase B Titer

Age Group	Normal Levels
Preschool children	1:60 units
School children	1:480 units
Adults	1:340 units

in children (Table 8.29). Antistreptolysin O is raised in 80% of children with acute rheumatic fever and in 20% of normal children. Sensitivity of ASO is 80%. A rising titer is strong evidence of recent streptococcal infection

(b) Anti-deoxyribonuclease B (anti-DNase B) titer—this will peak after 6–8 weeks of infection. Sensitivity of ASO in addition to anti-DNase B, antihyaluronidase and antistreptokinase is 95%. Normal levels of anti-DNase B titers are given in Table 8.30

(c) Positive throat culture—sensitivity of throat culture (25%–40%)

(d) Recent scarlet fever/streptococcal sore throat—within previous 45 days (residual manifestation such as desquamation of palms and soles)

(e) Rapid streptococcal antigen detection test—a positive rapid streptococcal antigen detection test will confirm the presence of streptococcal infection

Criteria for diagnosis of acute rheumatic fever

In the first episode, one major and two minor or two major criteria are required in the presence of evidence of antecedent streptococcal infection for the diagnosis of acute rheumatic fever. Recent streptococcal infection is indicated by markedly raised ASO titer or other streptococcal antibodies, or group A streptococcus on throat culture or history of scarlet fever.

Three special categories in which two major or one major and two minor criteria are not needed for diagnosis of rheumatic fever are as follows:

1. Chorea—when other causes are ruled out.
2. Indolent carditis—insidious or late onset carditis.
3. Rheumatic fever recurrence—in the presence of a documented RHD, even the presence of one criterion in the presence of supportive evidence of previous streptococcal infection suggests recurrence.

In the presence of the first two criteria, there is no requirement of supportive evidence of previous streptococcal infection.

Carditis

Carditis is seen in 50%–60% of children with rheumatic fever. It is one of the earliest features and develops within the first two weeks of the onset of rheumatic fever. It is a pancarditis and involves pericardium, myocardium and endocardium.

In *subclinical carditis,* the clinical examination is normal. However, the ECHO findings are abnormal. It does not fit as a major criterion. *Indolent carditis* presents as no or very few features of carditis.

Signs of Active Carditis

1. Endocarditis—mitral valve is most commonly affected followed by aortic and tricuspid valves in that order. Pulmonary valve is almost never involved in rheumatic carditis
   - Pansystolic murmur of mitral regurgitation
   - Early diastolic murmur of aortic regurgitation
2. Myocarditis
   - Cardiomegaly
   - Carey Coomb's murmur, a delayed diastolic murmur due to mitral valve involvement
   - CCF—unexplained
   - S_3 gallop due to cardiac failure
   - S_1 muffled or soft
   - Tachycardia disproportionate to the fever
   - Conduction defects, arrythmias and heart blocks

3. Pericarditis
   - Chest pain
   - Pericardial friction rub
   - Pericardial effusion (unexplained)

Symptoms

- Dyspnoea due to CCF
- Syncope
- Pain due to pericarditis

Severity

According to the severity, carditis can be divided into mild, moderate and severe (Table 8.31).

Rheumatic carditis should be differentiated from infective endocarditis. Their differentiating features are given in Table 8.32.

TABLE 8.31 Features of Carditis Based on Severity

Features	Mild Carditis	Moderate Carditis	Severe Carditis
Cardiomegaly	Absent	Present	Present
Complications	Nil	Cardiomegaly	CCF Pericardial effusion
Treatment	Aspirin	Steroids + Aspirin	Steroids + Aspirin
Bed rest	4 weeks	6 weeks	Till heart failure is controlled

TABLE 8.32 Differences between Rheumatic Carditis and Infective Endocarditis

Features	Rheumatic Carditis	Infective Endocarditis
Onset and duration	Acutely ill	Chronic
Fever	High grade	Low grade
Vegetations	Large	Small
Blood culture	Negative for streptococci	Causative agent
Verrucae		
Size	Valves	Ventricular wall
Appearance	Sessile	Pedunculated
Friability	Not friable	Friable, so easily dislodged
Prognosis	Valvular stenosis	Wall defects, aneurysms

Arthritis

Fleeting polyarthritis is an early feature of rheumatic fever. The child will be sick with high fever and may sweat excessively. Arthritis occurs when the antibody levels are high. Joints involved are knee, ankles, elbows and wrists in that order. The affected joints become red, hot and swollen. Even slight movement causes pain in the joint which lasts for 2–7 days in one joint before moving to the other. The joints are involved in quick succession. There is a dramatic response to salicylates. The child responds to aspirin within 12–24 hours (if it does not respond, another diagnosis should be considered). The severity of arthritis is not related to the degree of cardiac involvement. Even mild arthritis can be associated with extensive damage of the cardiac valves. These features are summarised in Box 8.3. Differentiating features between rheumatic and rheumatoid arthritis are given in Table 8.33.

Subcutaneous Nodules

These are late manifestations that occur in 10%–15% of the patients with rheumatic fever and appear

BOX 8.3 Features of rheumatic arthritis

A	Acute, painful, asymmetric, polyarthritis
B	Bone normal—no residual bone damage
C	Common in children Complete recovery
D	Dramatic response to salicylates
E	Early manifestation of rheumatic fever
F	Fleeting poly arthritis
G	Good prognosis—subsides spontaneously
H	High fever
I	Involves the large joints especially knees, ankles, elbows and the wrists
J	Joints are red, swollen and tender for a day to a week Jaccoud's arthritis (chronic postrheumatic fever arthritis involving small joints of hands and feet)
K	Knee joint—commonly involved
L	Large joints are involved
M	Migratory polyarthritis

TABLE 8.33 Differences between Rheumatic Arthritis and Rheumatoid Arthritis

Features	Rheumatic Arthritis	Rheumatoid Arthritis
Age	Occur in children >3 years usually 5–15 years	May occur in children <3 years also
Onset	Acute	Chronic
Duration of illness	Short	Long
Joints affected	Larger joints	Smaller joints
Spine, Temperomandibular Interphalangeal joints	Not affected	Usually affected
Symmetry	Asymmetrical	Symmetrical
Character of pain	Migratory	Non-migratory
Diurnal variation	Not seen	Stiffness more in the morning
Fever	Present, high grade	Low grade
Muscle spasm, wasting	Absent	Present
Carditis	50%–70% Carditis common	<10% Rarely pericardial effusion
Evidence of streptococcal infection—ASLO	Positive	Negative
RA factor	Negative	Positive
Course	Acute, resolves with treatment. There can be recurrence	Chronic course
Residual defects in the joints	Not present Mild deformities of metacarpophalangeal joints may be seen (Jaccoud's arthritis)	Present Swan neck deformity, Boutonniere deformity
Response to salicylates	Response within 12–24 hours	Slow, less response
Course	Recovers fast	Chronic course
X-ray	Normal	Abnormalities such as narrowing of space

around 3–6 weeks after the onset of the rheumatic fever. These are always associated with carditis. Ninety-five per cent of patients with subcutaneous nodules will have carditis. These nodules are small (0.2–2 cm) firm, non-tender and felt over the bony prominences at the following sites:

- Behind ears
- Occipital region
- Along the spine
- Along the extremities—extensor surfaces of elbow, hands and feet

It is very difficult to differentiate subcutaneous nodule in occipital region with a posterior triangular or cervical lymph node (which are very common in children with infections in the scalp). Biopsy settles the diagnosis, as the subcutaneous nodule contains Aschoff bodies. These appear in crops and disappear within 8–12 weeks.

Chorea

These are purposeless, involuntary choreiform movements of the hands, feet or the face. They manifest 3–6 months after the onset of acute rheumatic fever. By this time, all other signs may have disappeared. The following features are seen in rheumatic disease:

- Common in females
- Emotional lability may be the first feature
- Self-limiting—lasts for 2–6 weeks
- Spontaneous recovery occurs within a few months
- About 25% of patients with chorea develop rheumatic valve disease

Erythema Marginatum

This is an early manifestation of rheumatic fever.

It appears as transient, non-specific, non-pruritic, red macule with serpiginous margins. It manifests over the trunk and the upper arm. It is not visible in dark skinned patients. This is often associated with chronic carditis. The application of heat will increase the rash.

S	Serpiginous margins
I	Itching will be absent
T	Trunk is the main site
E	Evanescent Early manifestation

Other Manifestations of Rheumatic Disease

- Fatigue
- Epistaxis
- Abdominal pain
- Anaemia
- Skin rashes
- Respiratory problems such as pneumonia/pleuritis/pleurisy/pleural effusion

RECURRENCE OF RHEUMATIC FEVER

The risk is highest in the first few years after an attack. Young children are more likely to develop recurrences. The following features indicate the recurrence of rheumatic fever in a patient with established heart disease:

1. Endocarditis
   - Change in pre-existing murmur
   - New murmur
   - Evanescent murmur
2. Myocarditis
   - Worsening cardiomegaly
   - Worsening cardiac failure
3. Pericarditis
   - Chest pain
   - Pericardial friction rub
   - Pericardial effusion

Terminologies used in recurrence of rheumatic fever

Terminology	Conditions
Recurrence	A new episode following a new infection occurs at least 8 weeks after stopping the treatment.
Rebound	Manifestations of rheumatic fever within 4–6 weeks of stopping the treatment or tapering of drugs.
Relapse	Worsening symptoms while on treatment often presents with carditis.

INVESTIGATIONS

The following investigations are required for diagnosis and to rule out complications:

1. Total count—increased
2. Differential count—polymorphonuclear leucocytosis
3. Haemoglobin %—anaemia
4. ESR—raised in acute rheumatic fever. It may, however, be decreased in the following conditions even in the presence of rheumatic fever:
   (a) Congestive cardiac failure
   (b) Mild carditis
   (c) Chorea
5. Acute phase reactants
   (a) ESR—increased (remains so for 4–10 weeks)
   (b) C-reactive protein (acute phase reactant)—increased. It is a β-globulin which is increased in acute rheumatic fever. Absence of this increase rules out acute rheumatic fever. Normal value of C-reactive protein is 6 mg/dL
6. Evidence of preceding streptococcal infection
   (a) Antibodies against streptococcal infection—Antistreptolysin O (ASO) titer is increased. More than 333 Todd units per milliliter are significant in children. Rising titer is significant and is a strong evidence of acute rheumatic fever. This peaks by 3–6 weeks and remains high for 3–6 months. This

may be altered by antibiotics and steroids. Conditions in which ASO titer is negative in rheumatic fever are as follows (anti-DNase B and streptozyme tests help in diagnosis in these cases):

- In 20% of cases it will be negative (positive only in 80%)
- 7 days before and 5 weeks after the onset of rheumatic fever
- In rheumatic chorea (as this occurs only after about 6 months after the onset of rheumatic fever)
- Early treated cases
- Mild carditis
- Technical errors

(b) Other streptococcal antibodies are antihyaluronidase (AH), anti-streptokinase (ASK), antistreptozyme (ASTZ), anti-DNase B (antidiphosphopyridine-nucleotidase) and anti-NADase (antinicotinamide adenine-dinucleotidase). Antihyaluronidase and anti-DNase B are increased in rheumatic disease

(c) Positive throat culture

(d) Rapid streptococcal antigen detection test

Evidence of Carditis

- Chest X-ray—cardiomegaly and pulmonary congestion.
- ECG—prolongation of P-R interval, varying degrees of heart block, features of pericarditis, T-wave inversion and reduction in QRS voltages
- ECHO—cardiac dilatation, valve abnormalities and rheumatic vegetations on mitral leaflets

TREATMENT

The treatment is broadly classified into three phases, as discussed below:

1. Treatment of group A streptococcal infection
2. Suppressive therapy
3. Supportive therapy

Treatment of Group A Streptococcal Infection

Group A streptococcal infection is treated by the use of the following drugs:

- Procaine penicillin—4 lakh units intramuscularly twice daily for 10 days
- Oral penicillin-V—250 mg 6 hourly for 10 days
- Benzathine penicillin G—1.2 million units (>27 kg) or 0.6 million units (<27 kg) intramuscularly single dose after sensitivity test
- Azithromycin oral—12.5 mg/kg/day once daily for 5 days
- Cephalexin oral—15–20 mg/kg/dose twice daily for 10 days

Suppressive Therapy

Both aspirin and steroids are effective in suppressing the acute signs of inflammation (Table 8.34). Steroids may bring down the signs more rapidly than aspirin but there is a great tendency for them to reappear after discontinuation of the treatment. Drugs should be given after feeds and avoided in an empty stomach to prevent gastritis. Antacids should also be given along with the drugs.

1. Aspirin 100 mg/kg/day in four divided doses is given orally for 3–5 days followed by 75 mg/kg/day in four divided doses for the next 4–8 weeks depending on the response. Blood level should be maintained at 20–25 mg/dL. This relieves the symptoms of arthritis rapidly within 24 hours. Maximum dose should not exceed 10 g/day.
2. Steroids—indications are as follows:
   - Carditis with cardiomegaly
   - Congestive cardiac failure
   - Aspirin toxicity
   - Patients not responding to aspirin

Prednisolone is started in a dose of 1–2 mg/kg/day (60 mg/m^2/day). It is given in four divided doses for 2–3 weeks and then tapered by 5 mg/day every 3–4 days. Steroids should be continued until the ESR has returned to normal (usually 2 weeks) and finally tapered off over 2–4 weeks. Salicylates in a dose of 75 mg/kg/day in four divided doses should be started during the last week of corticosteroid therapy and given for 6 weeks to complete total 12 weeks.

Supportive Therapy

1. Bed rest—absolute bed rest is advised for at

TABLE 8.34 Treatment Schedule for Suppressive Therapy in Acute Rheumatic Fever

Condition	Drug	Dose	Duration
Arthritis ± mild carditis (without cardiomegaly)	Aspirin[a]	100 mg/kg/day orally in four divided doses	3–5 days
		Tapering dose 60–75 mg/kg/day orally	Tapering dose to be given for 4–8 weeks. depending on the response (ESR becomes normal)
Moderate to severe carditis (with cardiomegaly or CCF)	Prednisolone	2 mg/kg/day (max. 80 mg/day)	Till ESR normalises (2–3 weeks usually) Taper over 2–4 weeks Start aspirin 75 mg/day simultaneously as steroids are tapered and continued for 6 weeks to complete 12 weeks
Non-responders (no response to oral steroids)	Methyl Prednisolone (IV)	30 mg/kg/day	3 days

[a]If there is intolerance to aspirin, naproxen can be given in a dose of 10–20 mg/kg/day.
If there is no response to naproxen, steroids should be started.

least 2 weeks (Table 8.35). The duration of bed rest should be decided by the severity of symptoms and the markers of inflammation such as temperature, leucocyte count and ESR. It should be continued for 2–6 weeks after the ESR and temperature have returned to normal.

2. Hospitalisation—indications are as follows:
   - Moderate-to-severe carditis
   - Severe arthritis
   - Chorea
3. Treatment of cardiac complications—for patients with cardiac failure, digoxin, fluid and salt restriction, diuretics and oxygen are given. In presence of MR and AR, the patient may not respond to the medical treatment. In such cases, valve replacement can be considered. Pacemaker may be needed for treatment of heart block.

TABLE 8.35 Duration of Bed Rest during Treatment of Rheumatic Fever

Clinical Conditions	Duration of Bed Rest	Gradual Ambulation
No cardiac involvement	2–3 weeks	2 weeks
Carditis without CCF (no cardiomegaly)	4–6 weeks	4 weeks
Carditis with cardiomegaly	6 weeks	6 weeks
Carditis with CCF	Until CCF is controlled	3 months

COMPLICATIONS OF RHEUMATIC HEART DISEASE

Rheumatic heart disease can give rise to

- arrhythmias,
- congestive cardiac failure,
- infective endocarditis,
- rheumatic valvular heart disease such as established mitral regurgitation,
- recurrent infections and
- Sydenham chorea

PREVENTION OF RHEUMATIC FEVER

It consists of primary, secondary and tertiary prophylaxis.

Primary Prevention

It consists of early recognition and treatment of streptococcal tonsillopharyngitis (Table 8.36) by appropriate antibiotic therapy initiated before ninth day of symptoms. This will prevent first attack of rheumatic fever due to the pharyngitis. Tetracyclines or sulfa drugs should not be used for primary prevention because high percentage of streptococcal organisms is resistant to these drugs.

TABLE 8.36 Drugs Used for Primary Prevention of Rheumatic Fever

Agent	Dose	Mode	Duration
Benzathine penicillin G			
<27 kg (601b)	0.6 million units	Intramuscular	Single dose
>27 kg (601b)	1.2 million units	Intramuscular	Single dose
Penicillin V			
Children	250 mg q.i.d.	Orally	10 days
Adolescents and adults	500 mg t.i.d.	Orally	10 days
Azithromycin	12.5 mg/kg/day once daily	Oral	5 days
Cephalexin	15–20 mg/kg/dose b.i.d.	Orally	10 days

Secondary Prevention

The purpose of secondary prophylaxis is to prevent recurrent attacks of rheumatic fever. Secondary prophylaxis means prevention of colonisation of upper respiratory tract in individuals who already have had a previous attack of rheumatic fever or established RHD. Recurrence of rheumatic fever can be prevented by giving following antibiotics (Table 8.37):

- Intramuscular benzathine penicillin—the drug is given in a dose of 0.6 million units (for children weighing under 27 kg) and 1.2 million units (for children weighing above 27 kg) once in 15 and 21 days, respectively. Before giving the injection the patient should be tested for hypersensitivity reactions. Even if the child has not developed any reactions during the previous injections, there is a possibility of anaphylactic reactions. Hence, the drug sensitivity should be tested each and every time.
- Oral penicillin V 250 mg twice daily or erythromycin 20 mg/kg/dose twice daily. Tetracyclines should not be used for secondary prevention because high percentage of streptococcal organisms is resistant to tetracyclines.

TABLE 8.37 Drugs Used for Secondary Prevention of Rheumatic Fever

Agent	Dose	Mode	Dose Interval
Benzathine penicillin G			
<27 kg (601b)	0.6 million units	Intramuscular	Once every 15 days
>27 kg (601b)	1.2 M U million units	Intramuscular	Once every 21 days
Penicillin V			
Children	250 mg b.i.d.	Orally	Daily
Adolescents and adults	500 mg b.i.d.	Orally	Daily
With penicillin allergy			
Erythromycin	40 mg/kg/day b.i.d.	Orally	Daily

Duration of the Prophylaxis

The prophylaxis is given up to 21 years of age or 5 years from the last attack, whichever is earlier. If heart disease is present, prophylaxis should be given lifelong or at least up to the age of 40 years (Table 8.38). Attacks are rare after the age of 21, so the prophylaxis can be stopped after attaining this age. There should not have been any attack of rheumatic fever in the preceding 5 years before stopping the prophylaxis. In areas of higher prevalence of rheumatic fever where there is high exposure to streptococcal infection, the prophylaxis should be continued lifelong. Also, people of certain professions such as medical profession, teachers and those living in crowded conditions who are frequently exposed to streptococcal infections are prone for recurrence. They can be given lifelong prophylaxis.

Tertiary Prophylaxis

It is given to prevent development of infective endocarditis in children with rheumatic valvular lesions. Prophylactic antibiotics are given prior to

TABLE 8.38 Duration of Secondary Prophylaxis in Rheumatic Fever

Conditions	Duration of Prophylaxis Following One Attack of Rheumatic Fever
No carditis	21 years of age or 5 years from the last attack
Mild-to-moderate carditis	25 years of age or 10 years from the last attack
Severe carditis	Lifelong
RHD	Lifelong
Postinterventions	Lifelong

TABLE 8.39 Interventions for Valvular Heart Diseases

Conditions	Interventions
Mitral stenosis	Balloon mitral valvuloplasty
Mitral regurgitation	Valve repair or replacement[a]
Aortic stenosis	Surgical intervention in symptomatic cases
Aortic regurgitation	Prosthetic valve replacement

[a]Prosthetic valves used for mitral valve replacement—Starr–Edward valve (ball and cage type), Bjork–Shelly (tilting disc), St. Judes valves, bioprosthetic valves.

any surgical procedures such as dental extraction to prevent development of infective endocarditis. It also includes surgical correction of deformities of the cardiac valves or replacement of the valves along with rehabilitation to prevent further damage (Table 8.39).

USUAL COURSE OF RHEUMATIC FEVER

- Rheumatic fever usually occurs between the first and second decade of life.
- Asymptomatic valvular heart disease develops between the second and third decade. It becomes symptomatic between the third and fourth decade. From the fourth decade onwards, prognosis can be assessed based on grades of dyspnoea.
- Carditis can cause permanent cardiac damage. Mild carditis disappears rapidly in few weeks and severe carditis may last up to 2–6 months.
- Arthritis subsides in a few days to weeks even without treatment and does not cause any permanent damage.
- Chorea usually subsides in 2–3 months without any neurological sequelae.

PROGNOSIS

Prognosis depends on the age at detection, stage, presence, extent of heart lesion, number of previous attacks and the treatment given. Prognosis is poor when the child develops carditis. Cardiomegaly is a poor prognostic sign. Patients with rheumatic fever may develop chronic RHD. The heart valve undergoes progressive fibrosis. Fusion of the mitral valve commissures and shortening of the chordae tendinae can lead to MS with or without regurgitation. Similar changes can occur in aortic and tricuspid valves but less commonly.

MITRAL STENOSIS

The mitral valve is also called bicuspid valve as it contains two cusps—the anterior and the posterior leaflets. The normal mitral valve area is 4–6 cm^2 in adults. Mitral stenosis refers to the narrowing of inlet valve into the left ventricle so that there is an obstruction to the inflow of blood from the left atrium to the left ventricle during diastole. It is most commonly of rheumatic origin. It can also be congenital.

CLASSIFICATION

The stenosis can be of two types:

I. Organic—the mitral valve is stenosed due to fusion of commissures.
II. Functional—there is an increased blood flow through the normal mitral valve.

AETIOLOGY

Mitral stenosis may be congenital or acquired.

Congenital Mitral Stenosis

It is due to congenital malformation of one or more mitral valve components, for example, thickened leaflet margins, shortened and fibrosed chordae tendinae, abnormal chordal attachments and abnormal papillary muscle fusion. In contrast to the MS of acquired origin, the OS (caused by the opening of mitral valve) in congenital MS is usually absent as the valve leaflets are neither mobile nor flexible.

Congenital MS may be symmetric or asymmetric based on the chordal attachments to the papillary muscles. Asymmetric MS is often known as *parachute mitral valve*, as all the chordae are inserted predominantly onto a single papillary muscle, thus resembling the appearance of a parachute. This is usually associated with AS and coarctation of the aorta.

Acquired Mitral Stenosis

Rheumatic Origin

It is rare in small children, as it requires 5–10 years to develop after the initial attack of rheumatic fever. Mitral stenosis does not occur with initial carditis of rheumatic fever; rather it occurs with development of chronic RHD. Rheumatic fever usually occurs in the age group of 5–15 years. Four common forms of mitral valve fusion are seen following the rheumatic fever:

1. Commissural (30%)
2. Cuspal (15%)
3. Chordal (10%)
4. Combined (45%)

Other Causes

- SLE
- Rheumatoid arthritis
- Mucopolysaccharidosis—Hurler's syndrome
- Coxsackie virus
- Obstruction by individual pulmonary veins
- Endomyocardial fibrosis
- Drugs—methysergide therapy
- Amyloidosis
- Ball valve thrombosis
- Malignant carcinoid syndrome—the serotonin secreted from the carcinoid syndrome in the gastrointestinal tract, commonly in the appendix, is absorbed from the gut and reaches the right side of the heart causing damage to tricuspid valves (commonest). Rarely, this may affect mitral valve causing MS.

OBSTRUCTION TO LEFT VENTRICULAR INFLOW

The conditions generally associated with obstruction to left ventricle inflow are as follows:

- Cor triatriatum—the left atrium is divided into upper and lower compartments by an abnormal fibromuscular septum. This septum has a small opening and causes an obstruction to the pulmonary venous return and hence the left ventricle. It occurs due to abnormal insertion of the embryonic common pulmonary vein into the left atrium. The upper compartment is the dilated common pulmonary vein and the lower compartment is the true left atrium.
- Left atrial myxoma is usually pedunculated and causes obstruction to the flow through the mitral valve during diastole.

As congenital MS is very rare, only the acquired MS of rheumatic origin is being discussed.

PATHOGENESIS

The rheumatic disease causes valvulitis, which causes thickening and fibrosis of the cusps. It is a continuous process and continues into the adult life. As a result, the leaflets get fused at the commissures. This leads to stenosis of the mitral valve orifice. This is associated with a loud first heart sound and an OS. The blood flow through this stenosed mitral valve results in MDM. The mitral valve, which is pliable, develops calcification and fibrotic thickening. As this develops, the intensity of the first heart sound and the OS diminishes. The severity of the stenosis depends on the flow velocity during diastole and transmitral gradient as measured by Doppler echocardiography. If transvalvular flow gradient is denoted by '*a*' and flow rate by '*b*', then

$a = fnb$

Doubling of '*b*' will quadruple '*a*'.

CLINICAL FEATURES

These are signs and symptoms seen in cases of MS. History of rheumatic fever will be positive. In cases of asymptomatic MS, physical signs alone may be found in the early stages.

1. Symptoms due to heart failure and pulmonary congestion—the earliest symptoms are due to decreased cardiac output followed by those due to pulmonary congestion.
   - Fatigue and decreased exercise tolerance
   - Dyspnoea on exertion
   - Orthopnoea
   - Cough
   - Wheezing
   - Palpitation

BOX 8.4 Causes of haemoptysis in mitral stenosis

- Frank severe haemorrhage—pulmonary apoplexy, which is due to rupture of thin-walled bronchial artery or veins due to sudden rise in the left atrial pressure.
- Winter bronchitis—blood-stained sputum (chronic bronchitis)
  Acute pulmonary oedema—pink frothing due to rupture of alveolar capillaries
- Pulmonary infarction
- Anticoagulant therapy

- Chest pain
- Haemoptysis (Box 8.4)

2. Symptoms of systemic venous congestion—these occur with severe MS
   - Oedema
   - Ascites
   - Oliguria
3. Other symptoms
   - Recurrent bronchitis
   - Increased incidence of seizures due to cerebral emboli
   - Dilatation of left atrium leads to hoarseness of voice due to compression of the left recurrent laryngeal nerve. This is called Ortner's syndrome
   - Sudden death due to ball valve thrombus

Examination of Cardiovascular System

Relevant general examination findings are as follows:

- Facies—mitral facies, also known as malar flush, is characterised by pinkish purple patches on the cheeks which occur due to vasodilatation and are seen in MS
- Pulse—low volume pulse, directly proportional to the severity of the stenosis
- Respiratory rate—usually increased, except in mild MS
- BP—low
- JVP—prominent *a* waves

Inspection Findings

The position of the apical impulse is usually normal (unless associated with MR/AR).

Palpation Findings

- Apex beat, usually normal in position, tapping in character, is displaced outwards in RVH due to pulmonary hypertension. The apex beat is displaced downwards and outwards in LVH. Left ventricular hypertrophy occurs when the MS is associated with other cardiac defects such as MR, AR and AS.
- There is palpable P_2 in the second left ICS.
- Diastolic thrill is present over the mitral area.

Auscultation Findings

Auscultation should be done in all areas. Findings are present in mitral area and pulmonary area (Fig. 8.30).

Mitral Area. In mitral area, heart sounds, opening snap, middiastolic murmur and crescendo presystolic murmur should be checked.

1. Heart sounds

(a) Loud first heart sound (S_1)—there is a wide pressure gradient across the mitral valve. So the mitral valve leaflets are kept wide open till the end of the ventricular diastole. During the ventricular systole as the ventricle contracts, there is a wide excursion and forceful closure of the thickened mitral valves. This causes a loud first heart sound. Also, as the mitral valve closure is delayed, the mitral closure sound overlaps the tricuspid valve closure, causing a summation effect. S_1 is absent in the following cases:
   - Calcified valve
   - Atrial fibrillation
   - Rupture of sinus of Valsalva

(b) Opening snap—it is heard after the second sound. It is caused by opening of the mitral valve. It is best heard just internal to the apex. It results from early diastolic buckling of the anterior mitral leaflet which is due to elevated left atrial pressure. Opening snap is best heard in between the tricuspid and mitral areas, with diaphragm of the stethoscope, and with the

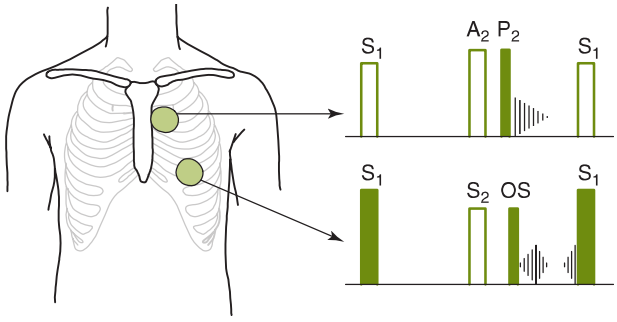


FIGURE 8.30 Auscultation findings in MS. S_1 is loud at the apex and is shown in black. In long-standing cases, early diastolic murmur is heard due to pulmonary regurgitation.

patient in a standing position. Presence of loud first heart sound and OS indicates the presence of pliable and non-calcified mitral valve. Opening snap may be soft or absent in

- Mild MS
- Severe MS
- Calcified MS
- Congenital MS
- Mitral stenosis with other associated lesions such as AS/AR

(c) Middiastolic murmur—it is low-pitched, middiastolic rumbling murmur, with presystolic accentuation of grade III intensity. It is best heard in the mitral area and is localised therein. It starts after the OS and is heard with the bell of the stethoscope in **e**xpiratory phase of respiration, with the patient lying in the left lateral position (Fig. 8.31). (Remember BELL—heard with *B*ell in the *E*xpiratory phase with patient lying in *L*eft *L*ateral position.)



FIGURE 8.31 Auscultation for MDM in a case of MS.

(d) Presystolic accentuation (crescendo presystolic murmur)—the atrial contraction leads to rapid filling phase of the ventricles, which occurs in the later part of the ventricular diastole. This rapid flow through a stenotic mitral valve leads to a presystolic accentuation. Presystolic accentuation is absent in the following conditions:

- Atrial fibrillation
- Left atrial failure
- Obstruction to left atrial outflow

Pulmonary Area

- The second heart sound is normally split with a loud pulmonary component.
- An ESM is heard in the pulmonary area with the development of pulmonary hypertension.
- A high frequency diastolic murmur of pulmonary regurgitation at the pulmonary area is known as Graham Steell's murmur.

Tricuspid Area. A functional pansystolic murmur at tricuspid area may be heard due to functional tricuspid regurgitation.

Examination of Other Systems

Nervous system—findings may include hemiplegia due to embolism, chorea due to rheumatic fever and Roth's spots in fundus examination.

Respiratory system—crepitations and rhonchi are seen in CCF and pulmonary congestion in moderate-to-severe MS.

Gastrointestinal system—liver will be enlarged, soft and tender in CCF; spleen will be enlarged and tender in infective endocarditis; and ascites may be present due to right-sided heart failure.

Severity of Mitral Stenosis

It is graded by various factors as discussed below:

1. Interval between the second heart sound and OS—it becomes narrower as the severity of the MS increases. Shorter the gap, the more severe is the stenosis
2. Duration of the MDM—longer the duration, the more severe is the stenosis. The length of the MDM is directly proportional to the severity of the MS
3. Severity of dyspnoea
4. Severe pulmonary hypertension indicates severe MS. Mild pulmonary hypertension may be present with mild, moderate or severe MS; but severe pulmonary hypertension occurs only with severe stenosis. Presence of Graham Steell murmur indicates severe MS
5. Left atrial enlargement in chest X-ray
6. ECG findings
   - Macruz index is used to diagnose atrial enlargement in ECG. Left atrial enlargement is associated with significant MS. Macruz index is based on the measurement of P-R interval, P wave duration and PR segment. In left atrial enlargement, P wave lengthens at the expense of PR segment, so that the ratio of P wave duration and PR segment is more than the maximal value of 1.6 (normal ratio is between 1.0 and 1.6; in right atrial enlargement, the ratio is less than normal value and in combined atrial enlargement, the ratio is normal)
   - Q-T interval is the measure of the time between the start of Q wave and the end of T wave in the ECG where the T wave merges with the isoelectric baseline. More the Q-T interval, the more severe is the stenosis
7. Mitral valve area is indirectly proportional to the severity of the stenosis

DIFFERENTIAL DIAGNOSIS

The following conditions cause MDM and may be confused with MS.

- Left atrial myxoma
- Cor triatriatum
- Ball valve thrombus of the left atrium
- Carey Coomb's murmur due to mitral valvulitis
- Diastolic flow murmur due to increased flow across the mitral valve in conditions such as VSD, PDA and severe MR
- Austin Flint murmur in AR

COMPLICATIONS

1. Back pressure effects
   - Acute pulmonary oedema and right ventricular failure in later stages
   - Pulmonary hypertension
   - Dilatation of left atrium will predispose to arrhythmias—atrial fibrillation, atrial flutter, ventricular or atrial premature beats
   - Recurrent respiratory tract infections
   - Tricuspid regurgitation
2. Infections
   - Infective endocarditis
   - Respiratory infections—pulmonary congestion predisposes to infection
3. Pressure effects
   - Dilatation of left atrium leads to hoarseness of voice due to compression of the left recurrent laryngeal nerve (Ortner's syndrome)
   - Compression of the oesophagus leads to dysphagia
   - Embolic manifestations, as the clot in the giant left atrium may get dislodged
   - Collapse of left lung
   - Dilatation of the pulmonary artery may press on the left main bronchus and predispose to bronchiectasis
   - Haemoptysis
   - Paraplegia due to erosion of the spine may occur
4. Thromboembolism is common in patients with atrial fibrillation (80%). This also occurs in

patients with sinus rhythm (may be due to transient atrial fibrillation/infective endocarditis). Incidence is directly proportional to age and the size of left appendage and indirectly proportional to the cardiac output. The incidence is also directly proportional to the size of the left atrium; larger the left atrium, the more is the incidence of thromboembolism. The embolism occurs in the cerebral arteries, peripheral arteries and the viscera. Sudden death is common in patients with ball valve thrombus.

INVESTIGATIONS

1. ECG
   (a) Electrocardiogram may be normal in the early stages.
   (b) Features of RVH—right axis deviation if there is secondary pulmonary hypertension.
   (c) Features of left atrial dilatation in the form of wide and notched *P* waves (*P*-mitrale).
   (d) Absence of *P* waves in the presence of atrial fibrillation. In atrial fibrillations, *f* waves replace *P* waves. Atrial fibrillation is rare in children.
2. Chest X-ray (posteroanterior view)
   (a) Left atrial enlargement—this causes the following changes in the X-ray:
      - Elevation of the left upper lobe bronchus.
      - Double shadow, that is, a shadow within the shadow. The dilated left atrium causes a shadow in the upper and outer border while that of the right ventricle causes a shadow in the lower and inner border.
      - Barium swallow studies show displacement of barium in the oesophagus due to dilated left atrium pressing the oesophagus. This is best seen in a chest X-ray of the right anterior oblique view after barium swallow.

   (b) Straightening of the left border of the heart is due to the dilated left atrial appendage and the pulmonary artery. Also, the aortic knuckle will be small. This is also called mitralisation of the heart.
   (c) Cardiomegaly—it is due to right ventricular enlargement.
   (d) Features of pulmonary hypertension—dilatation of the pulmonary artery near the hilum and pruning of the pulmonary artery at the peripheries (splayed carina).
   (e) Features of pulmonary venous congestion
      - Dilatation of the pulmonary veins is called inverted moustache sign.
      - Kerley B lines—these are fine, dense horizontal lines in the base of the lung at the costophrenic angles. These are due to stagnation of the blood causing distension of the interlobular septa and the lymphatics.
      - Kerley A lines are seen at apex, while Kerley C lines are seen at the hilar region.

   (f) Features of pulmonary haemosiderosis—multiple small opacities.
   (g) Calcification of the mitral valve.
3. ECHO—it shows cardiac enlargement, valve abnormalities and decreased ejection injection. The mitral valve has thickened immobile cusps and reduced valve area.
4. Cardiac catheterisation—to find out the pressure gradient between the left atrium and the left ventricle. It is also used to measure the pressure in the chambers and oxygen concentration.
5. Doppler studies—to study the direction of blood flow and the pressure gradient. Recurrence of rheumatic fever should be prevented.
6. Investigations for recurrence of rheumatic fever (see section *Investigations*, page 349).

TREATMENT

It is divided into medical management and surgical management.

Medical

It includes restriction of activities, according to severity of the condition. It consists of the following:

1. Treatment of cardiac failure

- Bed rest
- Salt-restricted diet
- Digoxin
- Diuretics
- Potassium supplementation to be given orally to prevent hypokalaemia

2. Rheumatic prophylaxis
3. Anticoagulants are given in cases with atrial fibrillation and/or if there is a history of thromboembolic event
4. Prophylaxis against infective endocarditis
5. Treatment of complications such as haemoptysis, acute pulmonary oedema and atrial fibrillation

Surgical

Indications for surgery in a child with MS are based on severity of symptoms and evidence of pulmonary hypertension. These are as follows:

- Symptomatic patients (NYHA functional classes II to IV) with moderate or severe MS (see Table 8.2))
- Established pulmonary hypertension (grades I to III)
- Ball valve thrombus in left atrium/recurrent systemic embolism
- Intractable CCF
- Arrhythmias not responding to treatment/established atrial fibrillation
- Infective endocarditis
- Progressive cardiomegaly
- Ejection fraction less than 15 mm (echocardiography)

Surgery is contraindicated in grade IV pulmonary hypertension.

Types of Procedures

1. Percutaneous balloon mitral valvuloplasty
2. Mitral valvotomy
   - Closed mitral valvotomy
   - Open mitral valvotomy
3. Mitral commisurotomy (closed or open)
4. Annuloplasty
5. Mitral valve replacement

Closed Mitral Valvotomy/Commisurotomy

Pre-requisites

- The valve should be pliable and non-calcified for the mitral valvotomy
- Preferred in patients with no associated MR
- Better results in children without severe thickening or subvalvar pathology

Indications

- Patients not responding to medical treatment
- Thromboembolic manifestations, even if they are asymptomatic
- Severe mitral stenosis

Contraindications

- Mitral stenosis with significant mitral incompetence
- Left atrial thrombosis
- Calcified mitral valve
- Restenosis
- Tight mitral stenosis

Open Mitral Valvotomy/Commisurotomy. This is preferred in children in whom closed intervention cannot be done. It is indicated in the presence of pure MS. The advantages of open commisurotomy are as follows:

- Valve commissures are opened.
- Any subvalvular fusion of papillary muscles or chordae tendinae can be relieved.
- Thrombi from left atrium can be removed.
- Left atrial appendage can be removed surgically to prevent a source of thromboemboli.

Percutaneous Balloon Valvuloplasty. It is preferred in patients on whom surgery cannot be performed. The criteria for performing this procedure are as follows:

- Isolated MS without associated MR
- Mobile and non-calcified valve
- Severe MS (valve area <1.5 cm^2 in adolescents and adults)
- No thrombus in left atrium
- Valve morphology should be suitable for valvuloplasty

Percutaneous balloon valvuloplasty may be followed by development of MR.

Mitral Valve Replacement. Open commisurotomy rather than valve replacement should be performed whenever possible. Mitral valve replacement is indicated in the following conditions:

- Rigid/calcified mitral valve
- Failure of closed mitral valvotomy/complications following it
- Valve morphology not suitable for valvuloplasty

Valves that can be used for replacement are as follows:

1. Prosthetic valves—tilting disc (preferred) and caged ball type. The disadvantage of using prosthetic valves for replacement is that prophylaxis for infective endocarditis and anticoagulants should be given lifelong.
   - Starr–Edwards's valve (caged ball and socket type)
   - Bjork–Shiley valve (tilting disc type)
   - St. Jude's (tilting disc, bileaflet).
2. Bioprosthesis—heterograft valve and porcine valve. These do not require anticoagulation but tend to deteriorate more rapidly. The advantage of using bioprosthetic valves is that the incidence of thromboembolic phenomenon is low. It should not be used in young patients because of its rapid deterioration.

Complications of Surgery

- Paravalvular leakage
- Thromboembolism
- Bleeding manifestations (due to use of anticoagulants)
- Haemolytic anaemia (due to the mechanical forces where the RBCs get damaged while the valve closes)

MITRAL REGURGITATION

Mitral valve closes during ventricular systole, thereby preventing blood flow into the left atrium during systole. Any destruction or deformity of the mitral valve results in flow of blood from the left ventricle back into the left atrium. This is known as MR.

Mitral incompetence is the commonest lesion in children with RHD. Males are more commonly affected than females. The defect in the valve can be due to congenital or acquired causes.

CAUSES

1. Congenital
   - Isolated
   - Associated with PDA, coarctation of aorta, VSD, corrected TGA and anomalous origin of left coronary artery from the pulmonary artery
2. Acquired
   - Rheumatic heart disease
   - Mitral valve prolapse syndrome

ASSOCIATED CONDITIONS

Mitral regurgitation may be present in association with the following conditions:

1. Corrected TGA
2. Endocardial fibroelastosis
3. Endocardial cushion defect
4. Ostium primum type of ASD
5. Congenital coarctation with MR
6. ASD (secundum) with floppy mitral valve
7. Connective tissue disorders
   - Ankylosing spondylitis
   - Rheumatoid arthritis
   - SLE (Libman–Sacks endocarditis)
   - Marfan's syndrome
   - Ehlers–Danlos syndrome
8. Mucopolysaccharidosis—Hurler's syndrome

Functional MR is common in children due to increased flow across the mitral valve.

PATHOLOGY

- Annulus dilated
- Deformed valve leaflets
- Short chordae tendinae
- Anomalous insertion of chordae tendinae
- Rupture of valve cusps/chordae tendinae/rupture of papillary muscles (infective endocarditis, injury—mitral valvotomy, postsurgical)
- Papillary muscle dysfunction
- Myxomatous degeneration of the mitral valve
- Prosthetic valve endocarditis

CLASSIFICATION

It is classified as acute and chronic according to the type of onset. This is given in Table 8.40.

HAEMODYNAMICS

The mitral valve closes during the onset of ventricular systole, thereby preventing the flow of blood from the left ventricle to the left atrium.

In MR, there is a systolic leak of blood into the left atrium. So the left atrial pressure increases during systole and decreases during diastole. Thus, the mean left atrial pressure stays normal. Hence, there is no increase in pulmonary venous pressure and no pulmonary congestion. If pulmonary congestion is present, it suggests acute MR or severe MR.

CLINICAL FEATURES

These depend on the severity of regurgitation. In mild MR, child is usually asymptomatic. In moderate to severe MR, child presents with the following symptoms:

- Poor weight gain
- Fatigue and exertional dyspnoea due to decreased systemic output
- Dyspnoea occurs late due to delayed pulmonary congestion. It occurs early in acute MR
- Palpitations due to atrial flutter, fibrillation

TABLE 8.40 Classification of Mitral Regurgitation

Onset	Causes
Acute	Infective endocarditis Acute rheumatic fever Trauma Rupture of chordae tendinae
Chronic	Rhematic heart disease Cardiomyopathy Connective tissue disorder • Ankylosing spondylitis • Rheumatoid arthritis • Systemic lupus erythematosus (Libman–Sacks endocarditis) • Marfan's syndrome • Ehlers–Danlos syndrome Amyloidosis

- Orthopnoea and PND (features of CCF)
- Dyspnoea, fatigue and syncope (features of pulmonary hypertension)
- Past history of rheumatic fever

According to the severity, MR is classified as mild, moderate and severe.

1. Mild—mild cases are asymptomatic. The following features are seen:
   - Pansystolic murmur
   - Apical impulse—normal
   - No pulmonary hypertension
   - Regurgitant volume <25%
   - No cardiomegaly
2. Moderate—child presents with fatigue and exertional dyspnoea due to reduced systemic output. The following features are seen:
   - Apical impulse—hyperdynamic
   - Pansystolic murmur
   - Pulmonary hypertension will occur later. This is because the left atrium is enlarged, so pulmonary hypertension does not occur earlier
   - Cardiomegaly
3. Severe—child usually presents with the following features:
   - Severe dyspnoea
   - Cardiomegaly—left atrial enlargement and LVH
   - Severe pulmonary hypertension
   - Parasternal heave—the greater the left parasternal movement, severe is the MR
   - Presence of a thrill
   - Hyperdynamic apical impulse
   - Late systolic pulsation in parasternal area
   - Wide split of the second heart sound S_2 (except in severe pulmonary hypertension)
   - S_3 gallop
   - Third heart sound (S_3) louder
   - Middiastolic murmur—louder and longer the murmur, severe is the MR

Examination of Cardiovascular System

Relevant general examination findings are as follows:

- Pulse—low volume, collapsing pulse
- BP—wide pulse pressure
- JVP—normal in absence of CCF

Inspection Findings

- Apical impulse—downwards and outwards
- Precordium—hyperkinetic in severe MR

Palpation Findings

- Apex is shifted downwards and outwards, when the LVH is present.
- Precordium is normal in mild mitral incompetence. Hyperkinetic precordium is seen in severe cases.
- Left parasternal heave may be present in the presence of RVH. Parasternal heave, outwards shift of the apical impulse and epigastric pulsations are seen in RVH.
- Systolic thrill is present over the mitral area due to regurgitation into left atrium.

Auscultation Findings

1. Heart sounds

- First sound is normal or soft.
- S_2 is normally split in mild MR and widely split in moderate or severe MR due to early aortic closure. Split disappears with the onset of failure.
- Loud S_3 is heard at the apex due to increased early and rapid filling of the left ventricle.

2. Murmurs (Fig. 8.32)

- Pansystolic murmur starts immediately after the first heart sound and continues through the second sound, until the left ventricular pressure falls below the left atrial pressure. The murmur is high pitched and soft blowing and is best heard with the diaphragm of the stethoscope. This murmur is best heard in the mitral area and is conducted to axilla or to the back when the anterior leaflet is involved. It may be conducted to the precordium when the posterior leaflet is involved, since the jet is directed anteriorly.
- Functional MDM due to increased flow across the mitral valve is heard at the apex. It starts with the third heart sound.
- Late systolic murmur occurs in MVP.

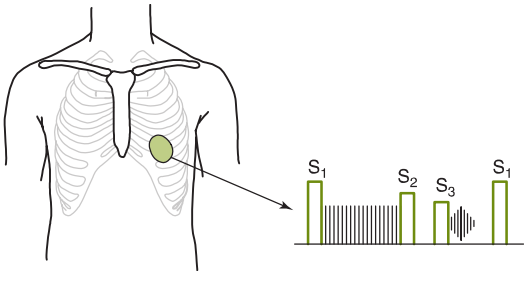


FIGURE 8.32 Auscultation findings in MR.

INVESTIGATIONS

1. Blood tests to detect rheumatic fever
   - Total and differential count
   - ESR
   - ASO titer
2. ECG
   - Normal in early stages
   - LVH
   - Left atrial dilatation
   - Biventricular hypertrophy
3. Chest X-ray
   - Cardiomegaly due to enlargement of left atrium and left ventricle
   - Right anterior oblique view shows elevation of left bronchus in a barium swallow study due to enlarged left atrium pushing the left bronchus
   - Calcification of annulus or leaflets
   - Signs of pulmonary venous hypertension
4. ECHO—M mode
   - Dilated left atrium
   - Dilated left ventricle
5. Cardiac catheterisation—dilated left atrium, left ventricle and MR
6. Selective left ventriculography
7. Colour Doppler

TREATMENT

Medical

Treatment of cardiac failure with diuretics and other decongestive measures (refer sections *Treatment*, page 380)

- Treatment of atrial fibrillation
- Anticoagulation in cases with atrial fibrillation
- Rheumatic fever prophylaxis—penicillin prophylaxis
- Infective endocarditis prophylaxis

Surgical—Valve Repair/ Replacement

Indications for Surgery

- Acute symptomatic MR secondary to a ruptured chordae tendinae or papillary muscle
- Intractable CCF—recurrent failure not responding to medical treatment
- Progressive deterioration in the left ventricular function
- Progressive cardiomegaly with symptoms
- Pulmonary hypertension

Types of Surgery

- Mitral valvuloplasty is preferred in children
- Prosthetic mitral valve replacement

Valves Used

Mechanical Valves

- Starr–Edward (caged ball type)
- St. Jude (tilting disc, bileaflet)
- Bjork–Shiley (tilting disc)

Bioprosthesis. The advantage of using bioprosthetic valves is that the incidence of thromboembolic phenomenon is low. It cannot be used in young patients because of its rapid deterioration.

FOLLOW-UP

Lifelong prophylaxis for infective endocarditis and lifelong use of anticoagulants are required after the valve replacement.

COMPLICATIONS DUE TO MR

- Congestive heart failure/acute left ventricular failure/right ventricular failure
- Infective endocarditis
- Arrhythmias—atrial fibrillation can occur but is not common
- Thromboembolic manifestations due to atrial dilatation
- Hoarseness and dysphagia due to dilated left atrium

MITRAL STENOSIS WITH MITRAL REGURGITATION

Mitral stenosis and mitral regurgitation may coexist in the same patient. It is important to find out which of these is the dominant lesion. The treatment should be modified accordingly. Table 8.41 gives the differentiating features between dominant MS and dominant MR lesions.

MITRAL VALVE PROLAPSE SYNDROME

It is also known as Barlow's syndrome, floppy valve syndrome, billowing mitral valve syndrome and midsystolic click syndrome. It refers to prolapse or ballooning of floppy enlarged mitral valves into the left atrium during systole. It is more common in females. It has an autosomal dominant inheritance with variable penetrance. It is commonly associated with the following conditions:

- Ehlers–Danlos syndrome
- Marfan's syndrome (nearly all patients with Marfan's syndrome have MVP)
- Turner's syndrome
- Pseudoxanthoma elasticum
- Straight back syndrome
- Osteogenesis imperfecta
- Pectus excavatum
- Scoliosis
- Rheumatic endocarditis
- Cardiomyopathy
- Secundum ASD
- Hypertrophic cardiomyopathy

PATHOLOGICAL CHANGES

There is myxomatous degeneration of the central spongiosa layer of one or both mitral valve tissues.

TABLE 8.41 Features Differentiating between Dominant Mitral Stenosis and Regurgitation

Features	Mitral Stenosis Dominant	Mitral Regurgitation Dominant
Clinical symptoms	Cough Haemoptysis Chest pain	Fatigue Exertional dyspnoea
Pulse	Low volume pulse	Large volume pulse
Blood pressure	Low systolic pressure	Normal
Apex	Normal or shifted outwards with right ventricular hypertrophy	Shifted downwards and outwards
Thrill at apex	Diastolic	Systolic
Apical impulse	Tapping apical impulse	Hyperdynamic apex
Ventricular dominance	Right ventricular hypertrophy Evidence of pulmonary hypertension. Left parasternal heave	Left ventricular hypertrophy
Auscultation		
• S_1 • S_2 • S_3	Loud Wide splitting S_3 absent	Soft Narrow split S_3 present
Added sound	Opening snap with narrow A_2—OS interval	Opening snap absent
Murmur • Diastolic • Systolic	 Long drawn middiastolic rumbling murmur with presystolic accentuation No murmur	 Short middiastolic flow murmur without presystolic accentuation Pansystolic murmur
Investigations		
• Chest X-ray • ECG • ECHO	Left atrial hypertrophy and right ventricular hypertrophy No left ventricular hypertrophy Right ventricular hypertrophy Reduced ejection fraction	Left ventricular hypertrophy and left atrial hypertrophy Left ventricular hypertrophy Left atrial dilatation Hyperdynamic left ventricle
Complications	Systemic embolisation Congestive heart failure Pulmonary oedema Atrial fibrillation	Chronic heart failure Infective endocarditis Thromboembolic manifestations

The posterior mitral leaflet is always involved. The valve is large and floppy. It is known as parachute mitral valve. The chordae tendinae may be long. In few cases, tricuspid valve may also be affected.

CLINICAL FEATURES

A child is usually asymptomatic. The condition is diagnosed on routine examination. Up to 40% of patients have dysautonomia. Symptoms of associated conditions such as Marfan's syndrome and hyperthyroidism may be seen. A child may present with the following clinical features:

- Chest pain
- Palpitations
- Arrhythmias
- Fatigue
- Syncope
- Autonomic dysfunction—panic attacks, anxiety, depression, irritable bowel and migraine headaches
- Neuropsychiatric manifestations

Examination of Cardiovascular System

Midsystolic click is best audible at the apex and may be followed by a late systolic murmur (Fig. 8.33). It may disappear on inspiration and is better heard by held expiration, leaning forwards, left decubitus position, sitting or standing. Various manoeuvres can alter the auscultatory findings in MVPS (Table 8.42).

INVESTIGATIONS

1. ECG
   - T wave inversion, non-specific ST changes in leads II, III and a VF

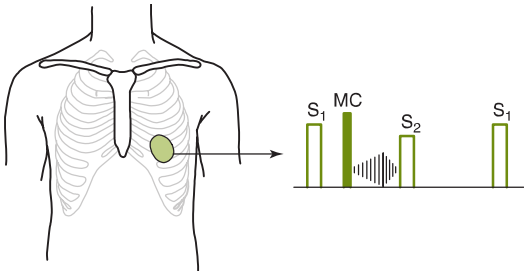


FIGURE 8.33 Auscultation findings in MVPS.

TABLE 8.42 Changes in Auscultatory Findings with Different Manoeuvres

S. N.	Manoeuvre	Effect on Left Ventricular Volume	Effect on Click and Murmur
1.	Standing Sitting Valsalva's strain phase Tachycardia Inhalation of amyl nitrite	Decreased	Click moves towards S_1 Murmur lengthens
2.	Squatting Hand grip exercise Valsalva's release phase Bradycardia Pressor agents Propranolol	Increased	Click moves towards S_2 Murmur shortens

   - Arrhythmias—supraventricular tachycardia
   - Prolonged Q-T interval
2. ECHO shows abrupt posterior movement of posterior mitral leaflet
3. Chest X-ray
   - Left atrial enlargement in patients with severe MR
   - Thoracoskeletal anomalies such as straight back (straight-back syndrome refers to loss of normal dorsal curvature of spine), pectus excavatum and scoliosis may be seen

TREATMENT

Medical

- β-blockers—propranolol
- Antibiotic prophylaxis for bacterial endocarditis
- Conduction disturbances should be treated with propranolol or phenytoin

Surgical

- Mitral valve repair should be done if the valve is almost normal without much damage.
- Mitral valve replacement should be done if the valve is damaged.

COMPLICATIONS

Most of the complications are due to embolism. There is an increased incidence of thrombus formation on the deformed mitral valve leaflet. This gets dislodged and obstructs the blood flow to the brain. This results in cerebrovascular accidents, cerebellar infarcts and focal neurological deficits. Other complications are as follows:

- Cardiac arrythmias
- Mitral regurgitation due to prolapse or rupture of chordae tendinae
- CHF
- Endocarditis
- Complete heart block
- Stroke
- Amaurosis fugax (transient monocular vision loss) and retinal arteriolar occlusion
- Infarction/gangrene

PROGNOSIS

Most children have a normal lifespan. However, sudden death can occur at any age.

Causes of sudden death in MVPS	
A	Arrhythmias—ventricular tachycardia and fibrillation
B	Blocks—complete heart block
C	Cerberovascular infarct/stroke due to embolism

Warning Signs

Presence of the following symptoms and signs is associated with sudden death. Hence, active intervention is needed if any of the following is seen to prevent sudden death of children with MVPS.

P	Palpitations
Q	Q-T interval prolonged in ECG
R	Rhythm disturbances—complex arrhythmia
S	Syncope

AORTIC STENOSIS

Aortic stenosis occurs due to narrowing of the aortic valve or its adjacent part of the aorta resulting in development of a pressure gradient between the left ventricle and the aorta. This comprises 5% of the congenital heart defects. Males are affected more than females.

AETIOLOGY

1. Congenital—associated with bicuspid aortic valve
2. Acquired
   - Rheumatic
   - Calcification of aortic valve

CLASSIFICATION

I. Based on the site of occurrence (Fig. 8.34)

1. *Valvular:* It consists of a dome-shaped diaphragm with an aperture and fused commissures. Bicuspid valve is more commonly associated with this type (Table 8.43). There may be a poststenotic dilatation of the ascending aorta. The causes are as follows:
   (a) Congenital—bicuspid aortic valve
   (b) Acquired
   - Rheumatic
   - Calcification of aortic valve
2. *Supravalvular:* There is a constriction either immediately above the sinus of Valsalva

TABLE 8.43 Conditions Associated with Aortic Stenosis

Type	Associated Conditions
Valvular	Bicuspid aortic valve
Supravalvular	William's syndrome Foetal hydantoin syndrome
Subvalvular	Patent ductus arteriosus Ventricular septal defect Coarctation of aorta

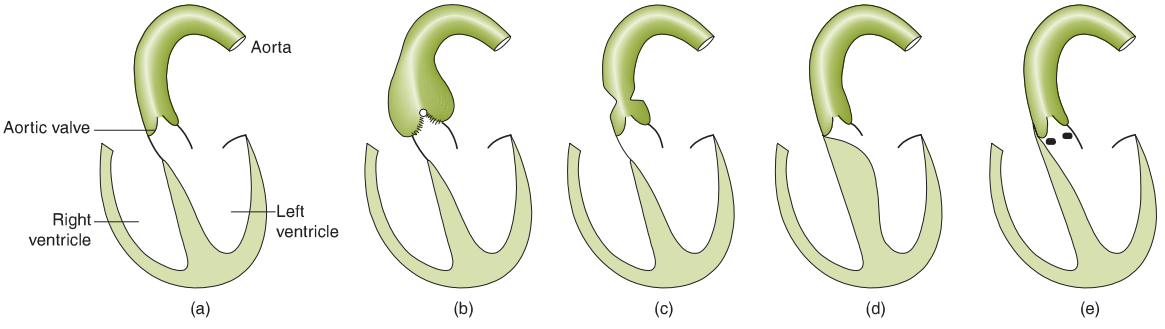


FIGURE 8.34 Types of AS. (a) Normal. (b) Valvular stenosis. (c) Supravalvular stenosis. (d) Idiopathic hypertrophic subaortic stenosis. (e) Discrete subaortic stenosis.

or there may be diffuse constriction of the ascending aorta. This is often associated with William's syndrome (Table 8.43). Predisposing conditions include rubella, hyperlipidaemia type II, postsurgical stenosis (surgery involving the aorta.). This type can be further classified according to the extent of stenosis.

(a) Hourglass
(b) Diffuse
(c) Discrete

3. *Subvalvular:* It may be due to any of the following conditions:
   (a) Simple diaphragm resulting in discrete subaortic stenosis.
   (b) Fibrous or fibromuscular obstruction to the outflow tract just beneath the aortic valve. The outflow tract thus appears like a long narrowing tunnel.
   (c) Hypertrophic cardiomyopathy (idiopathic hypertrophic subaortic stenosis)—hypertrophy of the interventricular septum is either symmetrical or asymmetrical. Intracavitary pressure gradient occurs during systole in some children with this condition due to anterior motion of the mitral valve against the hypertrophied septum. As the blood volume in the left ventricle decreases, the obstruction to the outflow increases. Arrhythmias can occur in these children.

II. Based on the size of aortic valve area—In children, the valve area is normalised to the body surface area. Normal valve area in children is 2 cm^2/m^2 of body surface area. In full-grown adolescents and adults, the normal aortic valve area is 3–4 cm^2. This is decreased in AS (Table 8.44).

TABLE 8.44 Classification of Aortic Stenosis on the Basis of Size of Aortic Valve Area

Classification	Valve Area (cm^2/m^2 of Body Surface) in Children	Valve Area (cm^2) in Adolescents and Adults
Mild stenosis	>0.8	>1.5
Moderate stenosis	0.5–0.8	1–1.5
Severe stenosis	<0. 4	<1

III. Based on the pressure gradient between left ventricle and aorta—cardiac catheterisation demonstrates the pressure difference between the left ventricle and the aorta. Classification of AS depending on the pressure gradient across the aortic valve is given below. A resting gradient of 60 mm Hg is an indication for surgery.

Severity	Pressure gradient across the aortic valve (mm Hg)
Mild stenosis	<50
Moderate stenosis	50–70
Severe stenosis	>70

HAEMODYNAMICS

As there is an obstruction to the left ventricular outflow, there is an increase in the left ventricular pressure. The ventricular systole is prolonged and the closure of the aortic valve is delayed. This leads to concentric hypertrophy of the left ventricle.

CLINICAL FEATURES

The following features are seen:

1. Classical triad
   - Exertional dyspnoea
   - Exertional angina
   - Exertional syncope
2. Fatigue
3. Exercise intolerance
4. Sudden death can occur in an asymptomatic child

Examination of Cardiovascular System

Relevant general examination findings are as follows:

1. Pulse
   - Pulsus parvus et tardus (slow rising pulse)—this pulse is characteristic of AS. It is a small volume pulse with a slow rising character and a late systolic peak. It may be associated with a carotid thrill

- Pulsus alternans—in the presence of left ventricular failure
- Pulsus bisferiens—when associated with AR

2. Blood pressure
   - Narrow pulse pressure
   - Systolic decapitation—as there is an obstruction to the left ventricular outflow, the systolic pressure does not rise above a certain level
   - Higher systolic pressure in the right arm as compared to the left arm is seen in supravalvular AS
3. Respiration—patient may be dyspnoeic
4. Facies—look for features of William's syndrome, that is, Elfin facies (prominent forehead, hypertelorism, low set ears, upturned nose, underdeveloped mandible, dental hypoplasia, pointed chin) with mental retardation. Supravalvular AS is common in such children

Cardiac Examination

Inspection Findings

- Apical impulse may be shifted outwards and downwards due to LVH.
- JVP—prominent *a* wave may be seen due to Bernheim effect. There is concentric hypertrophy of the left ventricle. The hypertrophied septum obliterates the right ventricle. Thus the blood from the right atrium cannot enter the right ventricle, instead the pressure is transmitted to the jugular vein.

Palpation Findings

- Apical impulse—heaving in nature due to LVH
- Systolic thrill—present in the aortic area and along the carotid arteries

Auscultation Findings

1. Heart sounds and added sounds (Fig. 8.35)

(a) First heart sound (S_1)—normal.
(b) Aortic ejection click—it occurs due to the opening of the aortic valve in valvular stenosis.
(c) Second heart sound (A_2P_2)
   - Delayed A_2—it occurs due to prolonged blood flow in the stenosed aortic valve.
   - Single S_2—S_2 may be single if A_2 is inaudible as in calcification or fibrosis of valve or immobility. Sometimes this aortic component of the second sound may overlap on the pulmonary component to produce a single second sound.

(d) Third heart sound (S_3)—it occurs due to development of LVF.
(e) Fourth heart sound (S_4)—it is a low-frequency sound heard in the late systolic period. It occurs when the left atrium contracts forcibly against a poorly compliant hypertrophied left ventricle.

2. Murmurs

(a) Ejection systolic murmur (rough, harsh) is best heard in the second and third right ICS in the aortic area and radiates to the carotids and axilla. The murmur is described as diamond shaped or crescendo decrescendo murmur when there is a peak at the middle of the systole, as compared

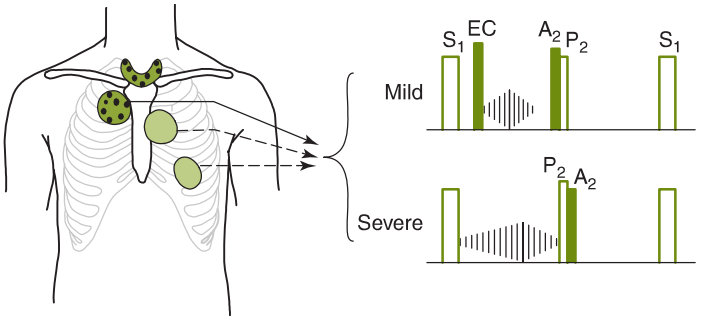


FIGURE 8.35 Auscultation findings in AS. Systolic thrill may be heard in the dotted area.

to the early and late systole. In congenital supravalvular AS, the murmur is preferentially conducted towards the right carotid (Coanda effect).

(b) Gallaverdin phenomenon—in calcified AS, the ejection midsystolic murmur is harsh in character. The musical high frequency component of this murmur is radiated to the apex or mitral area, while the harsh noisy component radiates to the neck due to high velocity jet in the ascending aorta. This dissociation between the noisy and musical components of the systolic murmur of AS is known as Gallaverdin phenomenon. This murmur is best heard with the diaphragm in full expiration with the child sitting and leaning forwards.

(c) Silent aortic stenosis—the murmur of AS is absent when AS is associated with CCF and/or MS.

3. Dynamic auscultation—the intensity of murmur increases or decreases with various manoeuvres done by the child.

Increased	Decreased
Inhalation of amyl nitrate With patient lying down Squatting Expiration	Valsalva manoeuvre

NATURAL COURSE OF AORTIC STENOSIS

The child may be asymptomatic and may develop symptoms suddenly. In children with severe AS, the following may be seen:

- Chest pain, syncope and even sudden death.
- Significant increases in the pressure gradient may occur. This may result in heart failure.
- Calcification of the valve cusps may result in worsening of the stenosis with ageing.
- Progressive worsening of AR in patients with discrete subvalvular AS.

INDICATORS FOR SEVERITY

- Symptomatic patients (syncope and angina)
- Symptoms of cardiac failure (paroxysmal nocturnal dyspnoea, orthopnoea and dyspnoea)
- Pulse—low volume, slow rising pulse (parvus et tardus)
- BP—the systolic pressure does not rise above 150 mm Hg in severe AS due to fixed left ventricular output (systolic decapitation). Narrower the pulse pressure (<30 mm Hg), severe is the stenosis
- Apical impulse—apical impulse is sustained and forceful in severe AS due to LVH
- Heart sounds—delayed or absent A_2, paradoxical splitting of S_2 and presence of fourth heart sound
- Heart murmur—later the peak of ESM, severe is the stenosis. Duration of murmur also indicates the severity. In severe AS, there is a prolonged murmur
- ECG—ST segment depression with T wave inversion due to left ventricular strain
- X-ray—enlarged left atrium
- Pressure gradient between the left ventricle and aorta during ventricular systole (>80 mm Hg)

A summary of these features is given in Box 8.5.

COMPLICATIONS

- Signs of cardiac failure—dyspnoea, pedal oedema, tender soft hepatomegaly and elevated JVP
- Acute pulmonary oedema
- Atrial fibrillation
- Pulmonary artery hypertension
- Infective endocarditis (rarely)
- The subvalvular stenosis may lead to progressive obstruction and AR
- Sudden cardiac death
- Severe AS in the intrauterine period is associated with hydrops foetalis
- Ischaemia or infarction of the heart

INVESTIGATIONS

1. ECG—it is completely normal in mild cases and even in some severe cases. The following changes may be seen in severe AS:
   - Left axis deviation
   - Left atrial dilatation
   - Left ventricular hypertrophy with left

BOX 8.5 Features of severe aortic stenosis

A	Anacrotic pulse—low volume Aortic pressure curve—early anacrotic notch, slow rising plateau, prolonged and delayed systolic upstroke, delayed dicrotic notch Area of aortic valve—<0.5 cm^2/m^2 Absent A_2 Atrial (left) enlargement (radiological finding) Atrial (left) pressure increased
B	Blood pressure—systolic decapitation—systolic blood pressure fails to rise, diastolic pressure may rise Pulse pressure—narrow pulse pressure(<30 mm Hg)
C	Cardiomegaly—left atrial enlargement
D	Delayed or absent A_2—paradoxical splitting of S_2 Duration of ejection systolic murmur—prolonged
E	Ejection systolic murmur—later the peak severe is the stenosis ECG—ST depression with T wave inversion
F	Failure symptoms—dyspnoea, chest pain
G	Gradient between the left ventricle and the aorta is more than 70 mm Hg With the onset of failure the gradient will be decreased because of low cardiac output Graded exercise testing—decreased capacity
H	Heart sounds—paradoxical splitting of second sound S_3, S_4 may be present
I	Intensification (late) of ejection systolic murmur

ventricular strain pattern—ST segment depression with T wave inversion
- First-degree heart block or complete heart block (due to calcification extending into the conducting system)

2. Chest X-ray
   - Usually normal
   - Left ventricular hypertrophy may be present. Cardiomegaly is seen in cases with CCF
   - Dilated ascending aorta or a prominent aortic knob may be seen in valvular AS due to poststenotic dilatation
   - Calcification of aortic valve in severe cases
   - Globular heart with mild left ventricular enlargement is seen in hypertrophic subaortic stenosis
3. ECHO
   - Site of obstruction can be identified
   - In bicuspid aortic valve, there will be an eccentric closure of the aortic valve
   - Fluttering of aortic valve is seen in subaortic stenosis
   - Concentric hypertrophy of left ventricle
   - In hypertrophic cardiomyopathy with subaortic obstruction, there will be a systolic anterior motion of the mitral leaflet
4. Doppler study is done to estimate the pressure gradient
5. Left cardiac catheterisation is done to estimate the magnitude of the pressure gradient

TREATMENT

If cardiac failure is present, it should be treated as described in section *Treatment*, page 360. Other measures of treatment have been discussed further.

Interventional Procedure

It consists of aortic valve balloon dilatation (AVBD).

Indications

- Aortic valve gradient of more than 50 mm Hg on Doppler echocardiography (even in the absence of symptoms).
- Infants with cardiac failure.
- Infants with severe AS and very low cardiac output (low forward flow results in low pressure gradient of 10–20 mm Hg across the aortic valve).

Assessment of Outcome

Outcome of AVBD can be assessed by monitoring the following parameters:

- Decrease in the aortic gradient
- Improvement in the left ventricular function
- Decrease in the ventricular hypertrophy

Complications of Balloon Dilatation

- Aortic regurgitation
- Femoral artery thrombosis
- Arrhythmias
- Damage to other cardiac structures

Surgical Repair

- Valve replacement—porcine and homograft valves are more prone to calcification in young adults. They, however, do not require anticoagulation. The mechanical prosthetic valves are long lasting and require anticoagulation.
- Ross procedure—this is an aorta–pulmonary translocation. The normal pulmonary valve is used to replace the abnormal aortic valve and the homograft valve is placed in the pulmonary artery. The homograft valve lasts for a longer time in the low pressure pulmonary circulation.
- Resection—discrete subaortic stenosis can be resected.

Indications

- Supravalvular AS—aortic valve gradient is greater than 50 mm Hg.
- Valvular AS—surgery should be done in all symptomatic patients or if there is left ventricular dysfunction as evidenced by ECHO.
- Subvalvular AS—immediate surgical repair should be done to prevent development of AR.

PROGNOSIS

The prognosis is good in children with mild and moderate stenosis. In children with severe stenosis, sudden death can occur.

AORTIC REGURGITATION

Aortic regurgitation occurs when there is an incompetence of aortic valve so that it fails to prevent the flow of blood from the aorta back into the left ventricle.

AETIOLOGY

The aetiological factors can be congenital or acquired as given below:

1. Congenital
   - Bicuspid aortic valve
   - Coarctation of aorta
   - Marfan's syndrome
   - Aneurysm of sinus of Valsalva
2. Acquired
   - Rheumatic
   - Syphilitic
   - Subacute bacterial endocarditis (SABE)
   - Rheumatoid arthritis
   - Ankylosing spondylitis
   - SLE
   - Dissecting aneurysm of ascending aorta
   - Traumatic rupture of cusp

HAEMODYANAMICS

With each systole the blood is pumped out of left ventricle into the aorta. During ventricular diastole there is regurgitation of blood back into the left ventricle. Also, there is a normal flow to the left ventricle from the left atrium. This results in a high-end diastolic volume in the left ventricle.

The volume output from the left ventricle is high. Also, there is a diastolic run off from the aorta into the left ventricle. This causes rapid filling and rapid emptying of the peripheral blood vessels. This phenomenon is responsible for the peripheral signs seen in AR.

CLINICAL FINDINGS

Symptoms

- Asymptomatic in mild cases
- Palpitation
- Decreased exercise tolerance
- Features of cardiac failure such as dyspnoea, orthopnoea and PND
- Chest pain

Signs

Peripheral Signs

1. Demusset sign—bobbing of the head with each heartbeat. The rapid blood flow in the carotids

pushes the head with each beat, thus leading to movement of the head up and down with each heartbeat
2. Light house sign—alternate flushing and blanching of the forehead
3. Becker's sign—pulsations seen in the retinal artery
4. Landolfi's sign—constriction and dilatation of pupils with heartbeats and not related to light reflex
5. Muller's sign—systolic pulsations seen in the uvula
6. Corrigan's sign—'dancing' carotids
7. Locomotor brachii—pulsations in the brachial artery seen prominently on the medial aspect of the arm, with the arm in a semiflexed position
8. Water-hammer pulse (collapsing pulse)—high volume pulse with collapse during the diastole is better felt in the radial artery with the arm elevated above the heart level (see section *Arterial Pulses*, page 290).
9. Quincke's sign—alternate flushing and blanching in the nail bed
10. Hill's sign—the systolic pressure in the lower limb is more than the systolic pressure in the upper limb; the pressure difference is more than 20 mm Hg. Normally, this pressure difference is less than 20 mm Hg. The severity of the AR can be assessed by measuring this difference

Severity of AR	Systolic pressure gradient (mm Hg)
Mild	20–40
Moderate	40–60
Severe	>60

11. Rosenbach's sign—pulsations of the liver
12. Gerhardt's sign—pulsations over the spleen
13. Traube's sign—pistol shot sound over the brachial/femoral artery. On proximal compression of the artery, systolic murmur is heard with the bell of the stethoscope. This is due to sudden distension of the artery
14. *D*uroziez's murmur—a *d*iastolic murmur is heard over the femoral artery with the diaphragm of the stethoscope when the femoral artery is compressed distally. It is due to blood flow in the reverse direction. (Four *D*s—*D*uroziez's murmur, *d*iastolic murmur, *d*istal compression and *d*iaphragm)
15. Duroziez's sign—systolic murmur on proximal compression and diastolic (Duroziez's) murmur on distal compression of the femoral arteries
16. Dennison's sign—pulsations of cervix
17. Oliver Cardavelli's sign—pulsations of larynx

Conditions in Which Peripheral Signs Are Absent

The peripheral signs may be absent in patients with acute onset AR as in infective endocarditis and trauma, or when it is associated with any of the following conditions:

- Aortic stenosis
- Tight mitral stenosis
- Congestive cardiac failure
- Systemic hypertension

Examination of Cardiovascular System

Relevant general examination findings are as follows:

- Pulse—high volume and collapsing in character (water-hammer pulse)
- BP—high systolic and low diastolic pressure (wide pulse pressure)

Cardiac Examination.

1. Inspection findings—apical impulse is displaced outwards and downwards due to the enlargement of both the ventricles.
2. Palpation findings
   (a) Apical impulse
      - Displaced outwards and downwards.
      - Hyperdynamic in character (due to volume overload, the pulse will be felt over more than one space).
3. Auscultation findings (Fig. 8.36)
   (a) Heart sounds
      - First heart sound (S_1)—decreased in intensity.

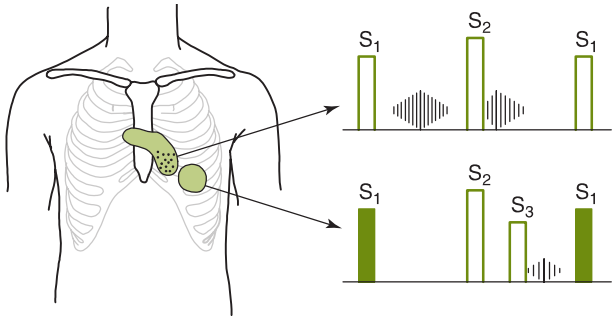


FIGURE 8.36 Auscultation findings in AR. S_1 is abnormally soft and is shown in black. The predominant murmur is diastolic murmur heard best in the left second and third intercostal space.

- Second heart sound (S_2)—normal or single. Soft S_2 in the aortic area in rheumatic AR.
- Third heart sound (S_3)—S_3 may be present.

(b) Murmurs

- Early diastolic murmur, high-pitched, soft blowing, decrescendo murmur. It is best heard with the diaphragm of the stethoscope in the aortic area (left second and third ICSs in parasternal area) with the patient sitting and leaning forwards in full expiration. The murmur may be conducted to the apex or the axilla when it fuses with the third heart sound and is called Cole–Cecil murmur. This murmur starts with the second sound and is greatest in the earlier part of the diastole. In the middiastole, the pressure in the aorta and the left ventricle becomes equal and there is no flow of blood into the ventricle from the aorta. The longer the murmur, the more severe is the regurgitation.
- A functional systolic murmur may be heard at the second right ICS due to an increased blood flow across the aortic valve. The regurgitated blood from the aorta will be added to the cardiac output and the stroke volume will be increased. This causes an increased flow in the aortic valve leading to a functional systolic murmur in the aortic area. A systolic murmur with thrill indicates the presence of an associated AS.
- Austin Flint murmur—this is a low-pitched MDM, heard in the mitral area in cases with severe AR. This is due to the impingement of the jet of the regurgitant blood from the aorta on the anterior mitral leaflet. This causes a relative MS, which gives rise to a MDM.
- Auscultation of other areas will be normal or the transmitted murmurs may be heard. In rheumatic AR, other valves may be involved and murmurs of MS or MR may be heard.

(c) Dynamic auscultation—the following manoeuvres cause change in murmur of AR:

- Early diastolic murmur of AR—it increases with child sitting and leaning forwards with breath held in expiration. It decreases with inhalation of amyl nitrate and Valsalva manoeuvre.
- Austin Flint murmur will be prominent with isometric exercise and use of vasopressors.

SEVERITY

The severity of AR is assessed by the following factors:

- Increased symptoms
- Pulsus bisferiens (best appreciated at the carotids)
- Hill's sign

- Biventricular hypertrophy (lateral and downward displacement of the apex)
- Marked peripheral signs
- Austin Flint murmur
- Duration of the diastolic murmur is more than two-thirds of the diastole
- Ejection systolic murmur due to functional AS
- Left ventricular dysfunction

Mnemonics for severity of AR

A	Austin Flint murmur
B	Biventricular hypertrophy
C	Carotid pulse—pulsus bisferiens
D	Duration of the diastolic murmur
E	Ejection systolic murmur due to functional AS
F	Failure—left ventricular dysfunction
G	Gerhardt's sign and other peripheral signs—marked
H	Hill's sign >60 mm Hg—severe
I	Increased symptoms

NATURAL HISTORY

- Asymptomatic for a long time
- Once the symptoms develop, the patient deteriorates rapidly

DIFFERENTIAL DIAGNOSIS

- Rupture of sinus of Valsalva—diastolic thrill may be present.
- Pulmonary regurgitation (Graham Steell's murmur) (Table 8.45)—can be confused with EDM of AR.
- MDM of MS (Table 8.46)—can be confused with Austin Flint murmur.

INVESTIGATIONS

1. To confirm the diagnosis

(a) ECG—normal or left ventricular enlargement
- Q waves in V_5, V_6
- Left atrial enlargement in long-standing cases

(b) Chest X-ray—cardiomegaly (massive left ventricular enlargement in chronic cases—cor bovinum)
- Prominent aortic knuckle due to aortic root dilatation
- Calcification of the aortic valve (in syphilitic, rheumatic and bicuspid aortic valve)
- Dilated descending aorta

(c) ECHO
- Dilated left ventricle
- Hyperdynamic left ventricle

TABLE 8.45 Differences between Early Diastolic Murmur of Aortic Regurgitation and Pulmonary Regurgitation

Features	Aortic Regurgitation	Pulmonary Regurgitation
Apical impulse	Hyperdynamic	Normal
Peripheral signs due to wide pulse pressure	Present	Absent
Murmur	High pitched	Low pitched
Site of murmur	Erb's area	Pulmonary area
Onset of murmur	Just after A_2	Wide gap after P_2
Direction of flow	Towards the apex	Towards the body of right ventricle. Hence, best audible along the left sternal border
Changes in relation to respiration	Best heard during expiration	Best heard during inspiration
Changes in intensity of murmur due to certain maneuvers	Amyl nitrate decreases the intensity of murmur Hand grip and intravenous phenylephrine decreases the murmur	No change with amyl nitrate or phenylepherine
Associated features	Left ventricular hypertrophy	Right ventricular hypertrophy

TABLE 8.46 Differentiating Features between Austin Flint Murmur and Middiastolic Murmur of Mitral Stenosis

Features	Middiastolic Murmur of Mitral Stenosis	Austin Flint Murmur
S_1	Loud	Normal
S_3	Absent	Present
Opening snap	Present	Absent
Ventricular hypertrophy	Right	Left
Complications	Atrial fibrillation	Left ventricular dysfunction
Dynamic auscultation	Valsalva manoeuvre will decrease the intensity of MDM due to decreased pressure gradient between the LA and LV	Amyl nitrate decreases the intensity of murmur

LA—left atrium, LV—left ventricle, MDM—middiastolic murmur.

(d) Cardiac catheterisation—dilated left ventricle
- Dilated aortic root
- Aortic regurgitation

2. To find out the aetiology

(a) Investigation for rheumatic fever—total count, differential count, ESR, ASO titer and CRP

TREATMENT

Medical

1. Asymptomatic patients—no restriction of activity is needed for mild cases
2. Symptomatic patients
   - Restriction of activities is needed for severe AR cases.
   - Antifailure treatment (refer section *Treatment*, page 380)
   - Rheumatic fever prophylaxis (refer section *Prevention of Rheumatic Fever*, page 351)
   - Infective endocarditis prophylaxis (refer section *Prevention*, page 391)

Surgical

- Valve replacement
- Surgical repair of the valve

Indications for Surgery

1. Regurgitation of >75% of the stroke volume
2. Severe symptoms
   - Anginal pain
   - Dyspnoea on exertion
3. In asymptomatic patients
   - Significant cardiomegaly (cardiothoracic ratio more than 55% on X-ray)
   - Ejection fraction less than 40%
4. Acute onset

Surgical Procedure

- Surgical procedure performed is Ross procedure (pulmonary root autograft aortic valve replacement).
- Bioprosthetic valves degenerate and calcify within 2–3 years.
- Prosthetic valves are the choice for severe AR. The types of valves available are ball and cage type, disc type and bileaflet type. Bjork–Shiley and the St. Jude prostheses are less suited for young patients.

Complications of Surgery

- Thromboembolism
- Haemolysis—chronic haemolysis due to mechanical valves
- Haemorrhage (anticoagulant induced)
- Endocarditis—prosthetic valve endocarditis
- Postoperative cardiac failure

COMPLICATIONS

- Congestive cardiac failure
- Infective endocarditis

PROGNOSIS

The presence of the following features is associated with bad prognosis:

- Anginal pain
- Congestive cardiac failure
- Multiple premature ventricular contractions (PVC)

AORTIC STENOSIS WITH AORTIC REGURGITATION

Aortic stenosis and aortic regurgitation may be present together. The clinical features depend on the lesion which is more prominent of the two (Table 8.47). Clinical features present in AS with AR are as follows:

- Apical impulse is hyperdynamic
- Pulsus bisferiens
- Murmur is best heard in the second aortic area

The following features indicate the development of AR in a child with AS:

- High volume pulse, pulsus bisferiens
- Wide pulse pressure
- Disappearance of systolic thrill

CONGESTIVE CARDIAC FAILURE

Congestive cardiac failure is a condition in which the heart is unable to maintain an output sufficient to meet the metabolic requirements of the tissues.

TABLE 8.47 Differentiating Features between Dominant Aortic Stenosis and Aortic Regurgitation

Features	Aortic Stenosis Dominant	Aortic Regurgitation Dominant
Clinical presentation	Effort angina Effort syncope Dyspnoea on exertion	Chest pain Dyspnoea Palpitation Fatigue
Pulse • Volume • Character	 Low volume Slow rising pulse	 High volume Collapsing pulse, pulsus bisferiens
Blood pressure	Systolic decapitation	High systolic Low diastolic
Pulse pressure	Narrow	Wide
Peripheral signs of aortic regurgitation	Absent	Present
Apex	Heaving	Hyperdynamic
Apical position	Normal	Down and out
Thrill	Systolic thrill in the aortic area and carotids	Systolic thrill rare. May be seen in functional aortic stenosis
S_3	Absent	May be present
S_4	May be present	Absent
Ejection click	Present	Rare
Murmur • Diastolic murmur • Systolic murmur	 Short diastolic murmur Ejection systolic murmur	 Early diastolic murmur Functional midsystolic ejection murmur
Investigations		
Chest X-ray	Normal size or left ventricular hypertrophy	Cardiomegaly Left ventricular hypertrophy
ECG	Left ventricular hypertrophy, left atrial hypertrophy Arrhythmias	Left ventricular hypertrophy
ECHO	Concentric hypertrophy of left ventricle Flow gradient low	Regurgitant flow in the aortic valve

AETIOLOGY

- Volume or pressure overload on a normal myocardium. This occurs in congenital diseases of the heart such as large left-to-right shunts or obstructive lesions of the left ventricle or right ventricle.
- Myocardial dysfunction due to various causes such as endocardial fibroelastosis, viral myocarditis and cardiomyopathy (may be associated with muscular dystrophy). Friedreich's ataxia may cause failure in older children and adolescents.
- Acquired diseases of the heart including myocarditis, acute or chronic RHD and infectious endocarditis.
- Arrhythmias, including paroxysmal atrial tachycardia, atrial fibrillation or flutter or complete heart block.
- Anomalous origin of left coronary artery from the pulmonary artery may cause CCF at around 2–3 months of age. This condition results in myocardial infarction in children.
- Non-cardiac causes, such as severe anaemia, thyrotoxicosis, systemic arteriovenous fistula, acute or chronic lung disease, glycogen storage disease, connective tissue disorders and neuromuscular disorders. Metabolic abnormalities such as hypoglycaemia and hypocalcaemia may cause failure in newborn infants.
- Renal causes—acute glomerulonephritis may cause hypertension, which results in CCF.
- Iatrogenic causes such as fluid overload, or cardiotoxic drugs such as doxorubicin (adriamycin [doxorubicin]) therapy.

Common causes of failure in various age groups are given in Table 8.48.

TABLE 8.48 Common Causes of Failure in Various Age Groups

Age Group	Causes of Cardiac Failure
Newborn	Hypoplastic left heart syndrome Aortic atresia and coarctation of aorta Patent ductus arteriosus Pulmonary stenosis/atresia Transposition of great vessels
1–2 months	Ventricular septal defect Aortic stenosis and coarctation of aorta Transposition of great vessels Endocardial cushion defects Patent ductus arteriosus Anomalous pulmonary venous connection
3–6 months	Ventricular septal defect Coarctation of aorta Endocardial fibroelastosis Transposition of great vessels
6–12 months	Endocardial fibroelastosis Ventricular septal defect
1–4 years	Carditis Anaemia Nephrotic syndrome and acute nephritis Endocardial fibroelastosis ASD or ventricular septal defect
>4 years	All the above causes and rheumatic heart diseases. Cardiomyopathy, pericarditis and myocarditis are more common in this age group

TYPES

According to the onset and pathophysiology, the heart failure may be classified as follows:

I. High output or low output failure
II. Acute or chronic failure
III. Right-sided or left-sided failure or biventricular failure
IV. Systolic or diastolic failure
V. With preserved ventricular function and abnormal ventricular function

According to the Cardiac Output

1. *High output failure* is a condition where there is high cardiac output with low vascular resistance. This type of failure is seen in the following conditions:
   - Hyperthyroidism (thyrotoxicosis)
   - Anaemia
   - Arteriovenous fistula
   - Wet Beriberi
2. *Low output failure* refers to a cardiac output <2.5–3.8 L/minute/m^2 during exertion. It is characterised by low cardiac output with high vascular resistance. This type of failure is seen in the following conditions:
   - Valvular heart disease
   - Hypertension

- Cardiomyopathy
- Pericardial disease
- Ischaemic heart disease (rare in children; can occur in conditions such as coronary vasculitis in Kawasaki's disease; anomalous origin of left coronary artery from the pulmonary artery; myocardial steal syndrome in which interarterial collaterals develop between the right and left coronary arteries; ectopic origin of coronary artery from the aorta with aberrant course)

According to the Onset of the Failure

1. *Acute heart failure* develops and worsens quickly. Sudden reduction in cardiac output leads to systemic hypotension without peripheral oedema. It occurs due to the following conditions:
   - Myocarditis
   - Valve rupture
   - Labile hypertension as in acute nephritic syndrome
2. *Chronic heart failure* develops slowly over a period of few weeks to months. Oedema is present even though the arterial pressure is well maintained. It occurs in the following conditions:
   - Progressive dilated cardiomyopathy
   - Multivalvular heart disease

According to the Ventricle Involved

1. *Right-sided failure* occurs in the following conditions:
   - Valvular PS
   - Pulmonary hypertension
2. *Left-sided failure* occurs in the following conditions:
   - AS (overload of ventricles)
   - Postmyocardial infarction (ventricle is weakened)—rare in children
3. *Biventricular failure* refers to failure of both the ventricles.

Timing of the Cardiac Cycle

1. *Systolic failure* is a condition where the heart fills normally but cannot pump enough blood into the aorta or the pulmonary artery due to decreased contractility. This results in accumulation of blood in the lungs, veins or both. This is also called heart failure with reduced ejection fraction. This is seen in the following conditions:
   - Myocarditis
   - Valvular lesions causing stenosis or regurgitation
   - Coronary artery disease
   - Myocardial ischaemia
   - Pulmonary disorders such as emphysema
   - Cardiomyopathy (as in Duchenne muscular dystrophy)
   - Drugs and toxic agents—amphetamine, alcohol, cocaine
2. *Diastolic failure* is due to inadequate filling of the heart due to improper relaxation of the heart. This is also called heart failure with preserved ejection fraction. It may be seen in the following conditions:
   - Hypertension
   - Ventricular hypertrophy causing stiffening of heart as in aortic valve stenosis
   - Constrictive pericarditis
   - Cardiomyopathy (infiltrative disorders—amyloidosis)
   - Infections

According to the Ventricular Function

1. *Ventricular function preserved*—left-to-right shunts (VSD, PDA)
2. *Abnormal ventricular function*
   - Pressure overload—aortic stenosis/pulmonary stenosis
   - Cardiomyopathy
   - Myocarditis
   - Ischaemia
   - Metabolic—hypocalcaemia

ASSESSMENT OF SEVERITY

NYHA Functional Classification

New York Heart Association developed a functional classification for patients with heart disease based on functional capacity.

Class	Features based on physical activity, symptoms and status at rest
I	*No limitation* of physical activities. Ordinary physical activities do not cause undue symptoms.
II	*Slight limitation* of physical activities. Ordinary physical activities cause fatigue, palpitation, angina or dyspnoea.
III	*Marked limitation* of physical activities. Less than ordinary physical activity causes fatigue, palpitation, angina or dyspnoea.
IV	*Inability* to carry any physical activity without discomfort. Symptoms occur even at rest.

ACC/AHA Stages

American Heart Association (AHA) and American College of Cardiology (ACC) gave certain guidelines and introduced four stages of heart failure based on structural damage and symptoms in 2005.

Group	Features based on structural changes in heart
A	High risk factors for developing heart failure but no identified functional or structural heart disorder; no signs and symptoms.
B	Developed structural heart disorder but no signs or symptoms.
C	Previous or current symptoms of heart failure in the presence of a structural heart problem, but managed with medical treatment.
D	Advanced structural heart disease with marked symptoms at rest and requiring hospital-based support such as heart transplant or palliative care.

CLINICAL FEATURES

The clinical features depend on various factors.

According to the Ventricle Affected

1. Features of left ventricular failure (pulmonary venous congestion)
   (a) Gallop rhythm—S_3 or S_4 is heard along with S_1 and S_2. This is called triple rhythm. This is associated with tachycardia in gallop rhythm
   - Pulsus alternans
   - Fine crepitations at the base of the lungs
   - Tachypnoea
   - Cough
   - Wheeze
   - Rales (basal)
   - Dyspnoea on exertion
   - Tachycardia
   - Fatigue
2. Features of right ventricular failure (systemic venous congestion) (Table 8.49)
   (a) Engorged neck veins due to systemic venous dilatation and raised JVP. The veins are pulsatile. (It is non-pulsatile in superior vena caval obstruction.)
   (b) Congestive hepatomegaly—soft, tender and may be pulsatile
   (c) Dependent oedema—pedal oedema in ambulant patients and over the sacral region in the bedridden patients. Massive accumulation can cause ascites and pleural effusion
   (d) Hepatojugular reflex is present

TABLE 8.49 Features of Cardiac Failure Depending on the Ventricle Affected

Left	Right	Biventricular Failure
Tachypnoea	JVP elevated	Cardiac enlargement
Tachycardia	Tachycardia	Tachycardia
Cough	Oedema	S_3 (gallop)
Wheeze	Liver enlargement	Peripheral cyanosis
Rales (basal)	Ascites	Small volume pulse
Dyspnoea on exertion	–	Poor weight gain

According to Age

The children at various age groups present with different clinical features.

1. Infants
   (a) Symptoms
   - Feeding difficulty
   - Poor weight gain
   - Irritability/excessive crying
   - Excessive perspiration
   - Wheezing
   - Noisy laboured breathing/fast breathing

   (b) Signs
   - Hepatomegaly
   - Cardiomegaly
   - Tachycardia
   - Gallop rhythm
   - Oedema, usually involving eyes, sacrum, legs and feet

2. Older children
   (a) Symptoms
   - Difficulty in breathing
   - Orthopnoea
   - Paroxysmal nocturnal dyspnoea
   - Fatigue and weakness due to reduction of blood supply to muscle

   (b) Signs
   - Tachycardia
   - Oedema is dependent and pitting type due to fluid retention and reduced venous flow
   - Hydrothorax and ascites
   - Congestive hepatomegaly
   - Engorged and pulsatile neck veins

3. All ages
   (a) Tachycardia
   (b) Gallop rhythm
   (c) Weak and thready pulse—pulse is low volume due to reduced stroke volume. The character of the pulse is pulsus alternans
   (d) Cardiomegaly
   (e) Increased sympathetic activity results in growth failure, perspiration and cold wet skin

INVESTIGATIONS

Confirmation of Diagnosis

- Chest X-ray—enlargement of heart
- ECHO

Detection of Aetiology

1. Chest X-ray—to differentiate between cardiac and respiratory disease.
2. ECG—changes will give clue to the diagnosis
   - Low voltage QRS complexes with ST-T wave abnormalities in myocardial inflammatory disease.
   - Arrhythmias—paroxysmal atria tachycardia, heart blocks.
   - Myocardial infarction changes are seen in anomalous origin of the left coronary artery from the pulmonary artery.
3. ECHO may be suggestive of cardiomyopathy. Vegetations may be present in infective endocarditis.
4. Blood culture to rule out infections such as infective endocarditis.
5. Haemoglobin for anaemia.
6. Thyroid function tests to detect hypothyroidism or hyperthyroidism.
7. Serum calcium—hypocalcaemia will result in CCF especially in newborns.
8. Arterial blood gas—hypoxia results in CCF especially in newborns.

Detection of Complications

- Blood urea is elevated in renal failure.
- Serum electrolytes—acidosis is seen in CCF.

TREATMENT

Treatment aims at the following measures:

1. Reducing the cardiac workload
2. Enhancing cardiac contractility
3. Improving cardiac performance by reducing the heart size (preload reduction)
4. Correction of the underlying and precipitating causes

Reduction of Cardiac Workload

General Measures

- Bed rest
- Propped up position
- Meals should be taken in small quantity
- Treatment of anaemia, if present
- Treatment of fever, if present

Specific Supportive Therapy

- Oxygen administration—humidified oxygen is given at a concentration of 40%–50%.
- Ventilatory support—it may be useful in some children for reducing the energy expenditure and oxygen demand. The peak end expiratory pressure should be modified according to the lung pathology. It should be high when there is pulmonary congestion and low in conditions with reduced pulmonary blood flow.
- Treat pulmonary oedema if present. It should be treated with diuretics.
- Intravenous fluids should be given after assessing the hydration status of the child and the presence of complications such as pulmonary oedema and renal failure. The maintenance fluids are usually given at two-thirds of the normal requirement. Further fluid restriction may be needed when cardiac failure is associated with oedema and dilutional hyponatraemia.
- Sedatives can be used in selective cases (restless child) after a proper assessment and maintaining SpO_2.
- Salt-restricted diet—sodium restriction in the food. High calorie, low sodium foods are given to older children.

Specific Drug Therapy

It is given to reduce the workload of the heart by reducing the afterload.

Vasodilator Therapy. This decreases peripheral resistance and thereby afterload on the heart. This improves cardiac output without any change in the contractility of the myocardium. Three groups of vasodilators are used (Table 8.50). They differ in their site of action as given below:

1. Venodilators—nitroglycerine and nitrates are venodilators. They help in reducing the venous congestion. They are useful in patients with elevated ventricular filling pressure, such as due to MS and AR.
2. Arteriolar vasodilators—hydralazine is an arteriolar smooth muscle relaxant. It is given in a dose of 0.5–1 mg/kg/day orally in three to four divided doses. It can also be given intravenously at 0.1–0.5 mg/kg.
3. Mixed vasodilators
   (a) Nitroprusside dilates both arteries and veins. Sodium nitroprusside is started in a dose of 0.5 µg/kg/minute (0.5–8 µg/kg/minute) and slowly increased until the arterial pressure falls by 10%. This drug should be given in an intensive care set up.
   (b) Prazosin is useful in patients with pulmonary hypertension.

Angiotensin Converting Enzyme Inhibitors. Angiotensin converting enzyme inhibitors (ACE inhibitors) prevent the conversion of angiotensin I to angiotensin II. Thereby it counteracts the salt and water retention, peripheral arterial and venous vasoconstriction and activation of sympathetic nervous system. These drugs reduce the afterload as well as the preload. They may cause a mild increase in the potassium levels. Hence, adding a diuretic with

TABLE 8.50 Vasodilators in CHF

Vasodilator	Drug	Complications/Side Effects
Venodilators	Nitroglycerine	Nitrites formed by metabolism oxidises haemoglobin to produce methaemoglobin
	Nitrates (isosorbide dinitrate)	Headache, giddiness, rash
Arteriolar vasodilators	Hydralazine	Hypotension, tachycardia, palpitation
Mixed vasodilators	Nitroprusside	Hypotension, liver dysfunction
	Nifedipine	Facial flushing, tachycardia
	Captopril	Agranulocytosis, impairment of renal function, hyperkalaemia
	Prazosin	Orthostatic hypotension

them may be beneficial. They are used as the first line of drugs in patients with cardiac failure which is not due to obstructive causes.

Mechanism of action:

- Adrenergic drive is decreased.
- It blocks the production of angiotensin II by competitive inhibition of angiotensin converting enzyme.
- Role of bradykinin—angiotensin converting enzyme is important for inactivation of a potent vasodilator bradykinin. Blockage of ACE results in increased bradykinin, which has a natriuretic effect. Other effects of bradykinin are decrease in afterload, increase in GFR, decrease in blood pressure and renal vasodilatation.

Drugs: Angiotensin converting enzyme inhibitors are indicated in cardiac failure due to ventricular dysfunction and hypertension.

- Captopril—the starting dose is 0.1 mg/kg/dose which can be increased gradually to 0.5–1 mg/kg/dose. Maximum dosage is 2 mg/kg/dose.
- Enalapril is used only in older children as it may cause renal dysfunction in neonates and infants. Dose is 0.1 mg/kg/dose given orally divided into two to four doses, not to exceed 0.5 mg/kg/dose.
- Lisinopril is given once daily.
- Ramipril is given 12 hourly.

Side effects: Abdominal pain, angioedema (rare), blurred vision, blood count decreased (agranulocytosis or neutropenia), cough, diarrhoea, maculopapular rashes, etc.

Precautions: Angiotensin converting enzyme inhibitors should not be used along with spironolactone because of the risk of hyperkalaemia. The patient should be recumbent to avoid first dose hypotension.

β-Blockers. They reduce the blood pressure in hypertensive children, thereby decreasing the afterload. They initially reduce the force of contraction of heart. Hence, they should be given only when the heart is stabilised with other drugs. It is often given along with ACE inhibitors. β-blockers block the action of norepinephrine. These are useful in diastolic failure as these drugs slow the heart rate and relax the cardiac muscle. β-blockers used are metoprolol and carvedilol. See Table 8.51 for dose.

TABLE 8.51 Dosage of Beta-Blockers

Drug	Dosage
Metoprolol	0.2–0.4 mg/kg/day in two divided doses; can be increased up to 1 mg/kg/day
Carvedilol	0.1 mg/kg/day in two divided doses; can be increased up to 2 mg/kg/day

Mechanism of action:

- They block the action of the circulating catecholamines.
- They also have antiarrhythmic effects.

Indications:

- Arrhythmias
- Hypertension
- Compensated cardiac failure

Adverse effects: A-V conduction heart blocks, bronchospasm, bradycardia, CHF (aggravated), constipation, dizziness, emesis (vomiting), failure (myocardial failure due to direct depression of heart), hyperglycaemia, hypotension, intermittent claudication and peripheral neuropathy

Contraindications:

- Acute decompensated cardiac failure
- Bronchial asthma
- Bradycardia—sick sinus syndrome
- Cardiogenic shock
- Hypotension
- Hypothyroidism

Enhancing Cardiac Contractility

Myocardial contractility is augmented by various drugs as given below:

- Digoxin
- Sympathomimetic amines—dopamine, dobutamine, epinephrine, isoproterenol, etc.
- Phosphodiesterase inhibitors—amrinone and milrinone

Digoxin

It increases the myocardial contractility. Digitalisation means to build up the blood levels of digoxin rapidly by giving large initial dose. Digoxin is given in a dose depending on the age of the child (Table 8.52). Half of this dose is given initially and one-fourth after 6

TABLE 8.52 Dose of Digoxin

Age	Oral Total Digitalising Dose (mg/kg)
Premature	0.02–0.025
Newborn	0.03–0.04
Infant or child	0.04–0.06
Adolescents	1.0–1.5

The total dose should not exceed 0.2–0.5 mg/24 hours. When digitalisation is done intravenously, 75% of the total oral dose should be given.

hours. The remaining one-fourth is given after the next 6 hours. Maintenance dose is 25% of the total digitalisation dose which should be given for 5 days in a week and should be given once in 24 hours. In children with mild CCF, directly maintenance dose can be started orally without giving the loading dose.

Adverse Effects. Digoxin has a narrow therapeutic range in children. Elevated serum digitalis level of >2–4 ng/mL in an infant and >1–2 ng/mL in older children is associated with digitalis toxicity. Adverse effects are as follows:

- Arrhythmias due to defects in impulse formation or conduction (supraventricular arrhythmias)—atrial and nodal ectopic beats, ventricular arrhythmias (ventricular bigeminy or trigeminy)
- Partial or complete heart blocks—prolongation of P-R interval
- Bradycardia (sinus bradycardia or sinoatrial block)
- Confusion, delirium, hallucinations, fatigue
- Visual disturbances such as blurred vision, photophobia, yellow/green vision, haloes, flashing lights
- Electrolyte imbalance (hypokalaemia)
- Nausea, vomiting and headache

Conditions Predisposing to Digitalis Toxicity

- Age—elderly, premature babies are more prone to toxicity
- Drug interactions—quinidine, verapamil, amiodarone
- Electrolyte imbalances—hypokalaemia, hypercalcaemia and hypomagnesaemia. Hypokalaemia enhances myocardial uptake of digitalis. Hypokalaemia can be precipitated by intravenous infusion of large doses of glucose, insulin or sodium bicarbonate. Digitalis acts synergistically with calcium by increasing the force of contraction of heart. Excess calcium will result in cardiac arrest in systole
- Kidney disease (decreases the excretion of digitalis)
- Liver disorders resulting in decreased detoxification
- Hypothyroidism
- Inflammatory changes/ischaemia in myocardium
- Hypoxia, acidosis and fasting (food in the stomach will slow the absorption of digoxin)

Contraindications

- Adverse effects to digoxin—hypersensitivity
- Blocks—AV blocks
- Carditis—acute myocarditis
- Decreased oxygen—hypoxia
- Electrolyte disorders
- Fibrillation (ventricular)
- Green vision (for drivers and pilots)
- Hypertrophic obstructive cardiomyopathy
- Hypothyroidism
- Infarction—acute myocardial infarction

Sympathomimetic Amines

- *Dopamine* is given at 2–10 µg/kg/minute by continuous infusion for inotropic support. (To give a dose of 10 µg/kg/minute, 30 mg/kg of the drug is added to 50 mL of normal saline and infused at 1 mL/hour.) At doses lesser than 5 µg/kg/minute, it causes renal vasodilatation. In high doses of 10 µg/kg/minute, the drug causes increased total peripheral resistance and increased heart rate.
- *Dobutamine* is used as an adjunct to dopamine therapy in a dose of 5–8 µg/kg/minute. It has direct inotropic effects with a moderate reduction in peripheral vascular resistance.
- *Epinephrine*—its action is to increase peripheral resistance via α-receptor-dependent vasoconstriction and to increase cardiac output via its binding to β-receptors. It is given at infusion rates of 0.04–1 mg/kg/minute.

- *Isoproterenol* is a β-adrenergic agonist. It increases the myocardial contractility and has positive chronotropic effect. It lowers vascular resistance in skeletal muscle, renal and mesenteric vascular beds. It lowers the diastolic BP; however, the increase in cardiac output is usually enough to maintain or raise mean BP. Renal blood flow is decreased in normotensive subjects but is markedly increased in patients with cardiogenic shock. It should be given in a dose of 0.1–0.5 μg/kg/minute.

Phosphodiesterase Inhibitors

- *Amrinone* (IV) has positive inotropic effect and peripheral vasodilator actions. It inhibits phosphodiesterase, and thereby prevents degradation of intracellular cAMP. It is given at 0.75 mg/kg intravenously as initial loading dose. This is followed by an infusion of 5–10 μg/kg/minute. Amrinone is hepatotoxic and can cause thrombocytopenia.
- *Milrinone* is given in a dose of 0.01–0.05 μg/kg as bolus or 0.01–1 μg/kg/minute in infusion.

Preload Reduction

Diuretics (e.g., furosemide, thiazides, metolazone) are used to reduce the preload. Venous dilators (e.g., nitroglycerin) can also reduce preload, but they are rarely used. The commonly used diuretics are as follows:

- *Furosemide* (loop diuretic) at 1 mg/kg/dose is given if there is pulmonary oedema. It may cause hypokalaemia. This should always be prevented by adding syrup potassium chloride, especially when a combination of digoxin and furosemide is being prescribed to the child, as it can cause fatal arrythmias.
- *Potassium sparing diuretics*—spironolactone, an aldosterone antagonist, does not lead to hypokalaemia. It is given in a dose of 2–3 mg/kg/day orally in two divided doses.
- *Others*—hydrochlorothiazide (2 mg/kg/day orally in two divided doses, metolazone (0.2 mg/kg/dose orally).

Correcting the Underlying and Precipitating Causes

1. Anaemia is corrected by packed cell (blood component) transfusion slowly at the rate of 10 mL/kg. Iron supplements may improve anaemia.
2. Treatment of the underlying causes such as arrhythmias, hypertension and thyrotoxicosis—atrial and ventricular fibrillation should be treated by cardioversion. Anticoagulants should be given prior to cardioversion if done electively; 2–6 watt-sec/kg is required for ventricular fibrillation.
3. Surgical corrections of cardiac defects—closure of PDA, VSD, etc.
4. Myocarditis should be treated carefully. The dose of digitalis should be reduced in this condition. Treatment should be supportive.
5. Precipitating factors such as fever and infection should be treated.
6. Surgeries for cardiomyopathy—improving the cardiac performance by surgical reduction of heart size in conditions such as dilated cardiomyopathy helps to prolong the life or delay the need for transplantation. Resection of a part of the ventricle will decrease the ventricular volume and wall stress, thereby improving the ejection fraction.
   - Batista procedure or reduction ventriculoplasty—the volume of left ventricle is reduced surgically to enhance the ventricular contraction.
   - Morrow's myectomy—transaortic approach is followed for HOCM which is resistant to medical treatment. The hypertrophied part of the interventricular septum is resected.
   - Cardiac transplantation—cardiomyopathy is the most common indication for cardiac transplantation. But it is also done in cases of severe congenital heart defects.

PREVENTION

The following steps should be followed to prevent the risk factors that lead to cardiac failure:

1. Life style modification.

2. Reduction in body weight.
3. Early diagnosis and treatment of the following disorders that can cause cardiac failure:
   - Heart diseases—valvular disorders, shunt disorders, coronary artery disease or blocks
   - Hypertension
   - Infections
   - Thyroid disorders
   - Anaemia
4. Avoiding drugs that can cause damage to the heart.

REFRACTORY HEART FAILURE

A child is said to have refractory heart failure when the heart failure does not improve with routine antifailure treatment.

CAUSES

1. Inflammatory causes of myocarditis
   - Idiopathic
   - Infections—myocarditis due to infections such as coxsackie virus A and B, Chaga's disease
   - Autoimmune—Kawasaki's disease
2. Endocrine
   - Hypothyroidism
   - Hyperthyroidism
   - Pheochromocytoma
   - Diabetes mellitus
3. Nutritional
   - Protein energy malnutrition—Kwashiorkor
   - Beriberi due to thiamine deficiency
   - Keshan disease due to selenium deficiency
4. Connective tissue disorders
   - SLE
   - Rheumatoid arthritis
5. Cardiomyopathy
   - Dilated cardiomyopathy
   - Drug induced cardiomyopathy, for example, Adriamycin (doxorubicin)
6. Muscular dystrophies
   - Duchenne
   - Becker's
7. Storage and infiltrative disorders
   - Amyloidosis
   - Haemochromatosis
   - Glycogen storage disease—Pompe's disease
   - Refsum's disease
   - Niemann–Pick disease
8. Coronary artery involvement
   - Anomalous origin of left coronary arteries.
   - Infarction of the myocardium is rarely seen in children and can be a cause of refractory failure.
9. Toxic
   - Antineoplastic
   - Radiation-induced cardiac toxicity
10. Metabolic causes—carnitine deficiency
11. Anatomical
    - Severe mitral stenosis
    - Severe aortic stenosis
    - Coronary arteries—anomalous origin of left coronary artery
12. Rhythm disorders—arrhythmias
13. Haematological causes
    - Severe anaemia
    - Sickle cell anaemia
14. Miscellaneous
    - Endomyocardial fibrosis
    - Neuromuscular disorders—Friedreich's ataxia

INVESTIGATIONS

1. Blood tests
   - Haemoglobin %
   - Peripheral blood smear
   - Serum electrolytes
   - Creatine phosphokinase (CPK) lactate dehydrogenase (LDH) are elevated in myocarditis
   - Thyroid function studies
2. ECG
3. Chest X-ray
4. ECHO—ejection fraction is poor, cardiac defects may be seen

5. Percutaneous endocardial muscle biopsy may show evidence of myocarditis
6. Immunologic studies for SLE
7. Investigations to rule out infections
   - IgM antibody for coxsackie virus
   - Polymerase chain reaction to identify viral DNA or RNA

TREATMENT

Treatment of refractory cardiac failure can be either pharmacological or non-pharmacological as detailed below.

1. Pharmacological therapeutic options
   (a) Infections should be treated with appropriate antibiotics after blood culture.
   (b) Steroids are given for immune-mediated dilated cardiomyopathy.
   (c) Propranolol and calcium channel blockers are useful in outflow obstruction.
2. Non-pharmacological therapeutic options
   (a) Assist devices—the advantages of this procedure is reduction in afterload and peak systolic wall tension, increased aortic root coronary perfusion pressure and reduction in myocardial oxygen demand, with improvement in cardiac output.
      - Ventricular assist devices (VADs) are used for a short period, so that time is allowed for the heart and lungs to recover.
      - Intra-aortic balloon pump (IABP)—the inflation is timed to coincide with the closure of the aortic valve and the deflation is timed to occur with the onset of the R wave on the ECG.

   (b) Biventricular pacing.
   (c) Blood/blood component transfusion—severe anaemia can be treated by packed cell transfusion in small volumes (4–5 mL/kg) or by exchange transfusion.
   (d) Cardiomyoplasty—latissimus dorsi or pectoralis muscle is surgically wrapped around the poorly functioning ventricle and initially placed to affect a good ventricular support.
   (e) Batista procedure to decrease the ventricular volume by ventricular volume reduction surgery. The volume of left ventricle is reduced surgically to enhance the ventricular contraction.
   (f) Pericardiocentesis for cardiac tamponade due to pericardial effusion.
   (g) Heart transplantation is used for the patients with intractable heart failure in conditions such as dilated cardiomyopathy.

COMPLICATIONS

1. Arrhythmias—atrial and ventricular arrhythmias are common. They may be due to electrolyte imbalances, underlying heart disease, circulating catecholamines and certain drugs such as digoxin.
2. Electrolyte imbalance—hypokalaemia occurs due to diuretic therapy. Hypokalaemia and hypernatraemia occur due to hyperaldosteronism (due to activation of renin angiotensin system).
3. Impaired liver function due to hepatic venous congestion and poor arterial perfusion.
4. Obstruction of blood vessels due to thromboembolism—deep vein thrombosis and pulmonary embolism due to low cardiac output. Bed rest and immobilisation of the patients also increases this risk.
5. Uraemia—it occurs due to poor renal perfusion.
6. Failure to thrive—chronic cardiac failure can lead to marked weight loss (cardiac cachexia) due to the following causes:
   - Anorexia
   - Basal metabolic rate—increased
   - Infections—repeated respiratory infection
   - Impaired absorption from gut due to gastrointestinal congestion
   - Increased sympathetic activity results in growth failure
   - Poor tissue perfusion and hypoxia
   - Chronic medication and hospitalisation

INFECTIVE ENDOCARDITIS

Infective endocarditis refers to infection of the endocardium. It is a common complication seen in children with cardiac defects. It is also rarely seen in some children with normal heart as a part of generalised septicaemia.

AETIOLOGY

It is caused by bacterial (acute and subacute) and non-bacterial agents. Table 8.53 lists the common organisms causing infective endocarditis in various conditions.

- Bacterial endocarditis: In a normal valve, the most common causative organism is *Staphylococcus aureus*. In an abnormal or injured valve, it is caused by organisms of low virulence.
- Non-bacterial thrombotic endocarditis: It is seen at the spot where the jet flow hits and damages the endothelium. It is caused by virus and fungi.

Bacterial Agents

The baceterial agents in paediatric infective endocarditis can affect either the native valves or the prosthetic valves.

1. Native valves
   (a) Common organisms
   - *Streptococcus viridians* group (*S. mutans, S. sanguis* and *S. mitis*)
   - *S. aureus*
   - Group D streptococcus (enterococcus) (*S. bovis* and *S. faecalis*)

   (b) Less common organisms
   - *S. pneumoniae*
   - *Haemophilus influenzae*
   - *S. epidermidis*
   - *Coxiella burnetii* (Q fever)
   - Culture-negative endocarditis (10% of cases)
2. Prosthetic valves—common organisms are *S. epidermidis, S. aureus, S. viridans Pseudomonas aeruginosa*

TABLE 8.53 Organisms Causing Infective Endocarditis in Various Conditions

Conditions	Organisms
Dental procedures	*S. viridans*
Normal valves	*S. aureus*
Gastrointestinal procedures	Group D *Enterococcus*
Genitourinary procedures	Group D *Enterococcus*
Intravenous drug abusers	*Pseudomonas aeruginosa, S. aureus, Serratia marcescens*
Immunosuppressed, severely debilitated	Fungal infections
Postcardiac surgery	Fungal infections

Culture-Negative Endocarditis

This condition is said to be present when the routine culture for infective endocarditis is negative. The following are the causes of culture-negative endocarditis:

- Partially treated cases
- Fungal endocarditis
- Libman–Sacks endocarditis in SLE
- As the organisms are shed intermittently, culture can be negative when the blood is taken in between the shedding of organisms

PREDISPOSING FACTORS

The occurrence of infective endocarditis depends on the virulence of the organism and the presence of cardiac defects. The children with the following high-risk factors are likely to develop infective endocarditis:

1. Heart disease
   - Congenital cardiac defects—in cases with cardiac defects where there is turbulence of blood flow, the endocardium gets injured. This forms a site for aggregation of the bacteria. All congenital heart defects except isolated secundum type ASD predispose to infective endocarditis. Commonest congenital defects are TOF, VSD, aortic valve disease, TGA, systemic to pulmonary artery shunt. Mitral valve prolapse syndrome with MR is considered a moderate risk category.

- Acquired—rheumatic heart disease.

2. Bacteraemia.
3. Cardiac surgery or presence of prosthetic valves in the heart.
4. Drug abuse (intravenous).
5. Interventions such as dental procedures (extraction of teeth), ear nose throat (ENT) procedures (adenoidectomy, tonsillectomy), cardiac catheterisation, intravascular catheters, genitourinary procedures, gastrointestinal procedures or rigid bronchoscopy may be followed by endocarditis.
6. Poor dental hygiene in children with congenital heart disease.
7. Immunodeficiency.
8. Infections at other sites such as teeth, ear and urinary tract also predispose to the spread of the infection to the heart.

PATHOGENESIS

The endocardium is damaged by the jet lesions from the shunts or the stenotic valves. The bacteria in the circulation get deposited in the injured endocardium. They are covered by fibrin and platelets and form vegetations. These vegetations are friable and get easily dislodged unlike the vegetations of rheumatic carditis.

CLINICAL FEATURES

A history of predisposing factors should be asked in any child in whom infective endocarditis is suspected.

Symptoms

- Fever with/without chills (unexplained fever in patients with a known heart defect)
- Chest pain
- Arthritis/arthralgia/myalgia
- Dyspnoea
- Malaise
- Night sweats
- Weight loss
- CNS manifestations such as stroke, seizures and headache
- CVS—symptoms of heart failure, arrhythmias
- Thromboembolic manifestations—transient ischaemic attacks, fits, stroke, focal neurological defects

Examination Findings

The following features are seen in head-to-toe examination:

1. General
   - Elevated temperature
   - Pallor (due to anaemia)
2. Skin lesions—the skin lesions are due to vasculitis produced by antigen–antibody complexes. these appear late in the disease and are not seen if the child is treated early
   - Necrotic skin lesions
   - Osler nodes—tender, pea-sized, intradermal nodes in the pads of fingers and toes
   - Janeway lesions—small, painless erythematous or haemorrhagic areas on the palms and soles
   - Splinter nail bed haemorrhages—linear haemorrhagic streaks beneath the nails
   - Petechiae—on the skin, mucous membranes and conjunctiva
3. Digits
   - Digital gangrene
   - Clubbing—tender and acute onset
4. Eye
   - Sudden loss of vision
   - Fundus findings—petechial haemorrhages, flame-shaped haemorrhages, Roth spots (retinal haemorrhages with pale centres located near the optic disc), papilloedema
5. Nervous system—neurological signs such as hemiplegia and focal neurological deficits from cerebral infarction
6. Lungs
   - Haemoptysis
   - Chest pain
7. Abdomen
   - Tender splenomegaly
   - Abdominal pain due to embolism in mesenteric vessels

- Left hypochondrial pain due to embolism in splenic vessels

8. Cardiovascular system
   - Tachycardia and arrhythmias
   - Changing cardiac signs—changing or new murmurs
   - Cardiac failure
9. Genitourinary system
   - Microscopic haematuria
   - Renal failure

INVESTIGATIONS

Investigations to be carried out in cases of infective endocarditis are as follows:

1. Complete blood count
   - Anaemia—normocytic and hypochromic
   - Leucocytosis
   - Thrombocytopenia
2. Erythrocyte sedimentation rate
   - Usually elevated
   - May be decreased with heart or renal failure
3. Urine examination—microscopic haematuria.
4. Blood culture—positive. Three blood cultures (about 10 mL each) are taken at half hour intervals under aseptic technique from different vein puncture sites and sent for culture. Both anaerobic and aerobic cultures are done. The release of the bacteria from the veruccae is intermittent. Hence, the diagnosis may be missed by doing only a single culture. Presumptive antibiotic therapy should be started once the blood is taken for culture. Prior use of antibiotics may be a cause for a negative culture. Positive blood culture gives a definite diagnosis of infective endocarditis
5. Culture from other sites—culture can also be done from the skin lesions, urine, synovial fluid, abscesses and cerebrospinal fluid in presence of meningitis
6. Elevated CRP
7. Immune complexes
   - Hypergammaglobulinaemia
   - Low complement levels
   - Cryoglobulinaemia
8. Rheumatoid factor may be positive in 50% cases
9. Azotaemia, high creatinine (glomerulonephritis)
10. Other findings
    - Mild proteinuria (due to nephritis, an immunological phenomenon)
    - Mild hyperbilirubinaemia may be present
    - ECG—heart blocks, if the septum is involved
    - Bone marrow culture and serological studies may be helpful in culture-negative cases
11. Echocardiography shows evidence of vegetations over the valve or the walls of the ventricles. The predisposing cardiac defects may be visualised. Small vegetations can be diagnosed by transesophageal echocardiography. Other associated findings such as prosthetic valve dysfunction or leak, or myocardial abscess can also be seen

TREATMENT

Treatment of infective endocarditis consists of medical management and surgical management.

Medical

Antibiotics are given according to the sensitivity of the organism isolated in blood culture. While awaiting blood culture, broad spectrum antibiotics which have gram-positive as well as gram-negative coverage should be started, for example third-generation cephalosporin with an aminoglycoside. Drug therapy for infective endocarditis according to the causative organism is given in Table 8.54.

Surgical

Indications for surgery are as follows:

1. Absolute indications
   - Refractory cardiac failure
   - Recurrent systemic emboli
   - Refractory infections (not responding to antibiotics in a week or blood has not become sterile)
   - Progressive intracardiac spread

TABLE 8.54 Drug Therapy for Infective Endocarditis

Causative organism	Drug of Choice	Dose	Route	Duration (weeks)
S. viridians	Penicillin G	2,00,000–3,00,000 units/kg/day	IV	4–6
S. aureus	Nafcillin	200 mg/kg/day (6 hourly)	IV	6–8
S. aureus (methicillin resistant)	Vancomycin	40 mg/kg/day (6 hourly)	IV	6–8
Haemophilus species	Ampicillin + Gentamycin	300 mg/kg/day (6 hourly) 2–4 mg/kg /day	IV IV	4–6 2–4
Enterococcus	Ampicillin + Gentamycin	300 mg/kg/day 2–4 mg/kg /day (max. 80 mg/day)	IV IV	4–6 2
Fungal	Amphotericin B and flucytosine	4–6 mg/kg/day (colloidal dispersion) + 50 mg/kg 6 hourly	IV IV	1

- Large vegetation causing obstruction
- Fungal vegetations as a result of fungal endocarditis and not responding to antifungal treatment

2. Relative indications—moderate CCF with severe AR or severe MR.

COMPLICATIONS

Complications of infective endocarditis

A	Acquired VSD Arrhythmias Arterial aneurysm
B	Blocks due to involvement of conducting fibres
C	Chordae tendinae—rupture Cardiac failure
D	Damage to the valve cusps (rupture of sinus of Valsalva)
E	Embolic manifestations—mesenteric infarcts, thromboembolic manifestations—renal infarct with haematuria, blurred vision, focal neurological deficits, gangrene of digits, ischaemic pain and loss of distal pulse
F	Focal neurological deficits
G	Glomerulonephritis—immune complex mediated Gangrene of digits
H	Haematuria (renal infarct)
I	Infection—metastatic infection (meningitis, arthritis, pericarditis, abscesses, septic pulmonary emboli) Injury to the myocardium, rupture of the chordae tendinae, mycotic aneurysm
J	Joints—arthritis Janeway lesions
K	Kidney—abscess, immune complex nephritis, focal glomerulonephritis, nephritic syndrome
L	Large vegetations—obstruction due to large vegetations
M	Mycotic aneurysms Myocardial abscess Myocarditis (toxic)
N	Nephrotic syndrome
O	Osler nodes Osteomyelitis
P	Pericarditis Pulmonary emboli

PROGNOSIS

Right-sided infective endocarditis has a more favourable prognosis than the left-sided infective endocarditis. This is because the left-sided vegetations can embolise to the systemic circulation directly while the vegetations of the right side get filtered in the pulmonary vessels.

Prognostic Indicators

The prognosis is poor in the following conditions:

- Culture-negative endocarditis
- Prosthetic valve endocarditis
- Involvement of multiple valves
- CCF

PREVENTION

The minor procedures such as dental extraction and genitourinary tract instrumentation predispose to infective endocarditis. Therefore, these procedures should be preceded by administration of antibiotics in high and moderate risk groups (Box 8.6). Endocarditis prophylaxis is recommended for the following procedures:

1. Dental
   - Tooth extraction
   - Periodontal procedures such as scaling and root planning
   - Dental implant placement
   - Root canal instrumentation
   - Initial placement of orthodontic bands (not brackets)
   - Intraligamentary local anaesthesia injections
   - Prophylactic cleaning of teeth with bleeding
2. Respiratory tract
   - Tonsillectomy
   - Adenoidectomy
   - Bronchoscopy
3. Gastrointestinal
   - Endoscopy
   - Endoscopic retrograde cholangiopancreatography (ERCP)
   - Surgical operations

BOX 8.6 Risk groups for infective endocarditis

High-risk group

- Prosthetic heart valves
- Previous endocarditis
- Complex cyanotic congenital heart disease—TGA, TOF, single ventricle
- Surgically constructed systemic to pulmonary artery shunt

Moderate-risk group

- Other congenital heart diseases such as VSD
- Rheumatic heart disease
- Hypertrophic cardiomyopathy
- Mitral valve prolapse syndrome with mitral regurgitation

4. Genitourinary
   - Cystoscopy
   - Vaginal delivery

Prophylaxis is not recommended in the following cases:

- Isolated secundum ASD
- Surgical repair of ASD, VSD and PDA
- Beyond 6 months after septal repair
- Previous Kawasaki's disease without valve dysfunction
- Cardiac pacemakers
- Implanted defibrillators

Drug Recommendations in Prevention

The drug recommendations for prevention of endocarditis are given in Tables 8.55 and 8.56.

EISENMENGER'S COMPLEX/SYNDROME

This is a condition where children with untreated left-to-right shunt lesions develop features of bidirectional or right-to-left shunt due to development of POVD. Conditions associated with Eisenmenger's complex/syndrome are

- Ventricular septal defect
- Atrial septal defect

TABLE 8.55 Antibiotic Prophylaxis in Dental Procedures

Drug	Dose	Route
Amoxicillin	50 mg/kg 1 hour before the procedure and 25 mg/kg 6 hours after the initial dose	Oral
Erythromycin	20 mg/kg 2 hours before the procedure and 10 mg/kg 6 hours after the initial dose	Oral
Ampicillin and gentamycin (in high-risk patients)	Ampicillin (50 mg/kg) and gentamycin (2 mg/kg) 30 minutes before the procedure	IM or IV
Vancomycin (in patients allergic to penicillin)	20 mg/kg can be infused 1 hour before the procedure	IV

TABLE 8.56 Antibiotic Prophylaxis in Genitourinary Surgery or Instrumentation

Drug	Dose	Route
Ampicillin and gentamycin	Ampicillin (50 mg/kg) and gentamycin (2 mg/kg) 30 minutes before the procedure	IM or IV
Vancomycin and gentamycin (in children who are allergic to penicillin)	Vancomycin 20 mg/kg Gentamycin 2 mg/kg 30 minutes before the procedure	IV
Amoxicillin (in low risk patients)	50 mg/kg 1 hour before the procedure and 25 mg/kg 6 hours later	Oral

- Patent ductus arteriosus
- Aortopulmonary shunts

PATHOGENESIS

1. Eisenmenger's syndrome—shunting of blood from the left-to-right side of the circulation leads to an increase in the pulmonary artery flow in patients with VSD, PDA or ASD. This predisposes to pulmonary hypertension. If the shunt is closed before permanent changes in the pulmonary arterioles occur, the pulmonary pressure comes down to normal. After a certain stage, the pulmonary pressure continues to increase even if the shunt is closed. Irreversible pulmonary hypertension develops due to permanent changes in the pulmonary vasculature POVD. It also results in reversal of left-to-right shunt. Eisenmenger's syndrome consists of severe pulmonary hypertension and cyanosis due to reversal of left-to-right shunt.
2. Eisenmenger's complex—when the above complications are seen in a child with VSD, it is known as Eisenmenger's complex.

CLINICAL FEATURES

Symptoms

- Dyspnoea
- Chest pain
- Haemoptysis
- Effort intolerance
- Fatiguability

Signs

- Cyanosis—central
- Differential cyanosis (PDA)
- Clubbing
- Failure to thrive (due to congenital heart disease)
- Hepatomegaly

Examination of Cardiovascular System

Inspection

- Bulging precordium
- JVP—jugular vein engorged
- *v* wave prominent in tricuspid regurgitation
- Epigastric pulsations

Palpation

- Parasternal impulse (right ventricle)
- Palpable S_2

Auscultation

1. First heart sound—normal
2. Second heart sound—P_2 accentuated
3. Few patients may develop pulmonary or tricuspid

regurgitation. The auscultatory findings in such patients are

- Graham Steell murmur—high-pitched EDM heard best at the left sternal edge in the second ICS with the patient in full inspiration (pulmonary regurgitation).
- Carvallo's sign—murmur of VSD or PDA disappears; pansystolic murmur of tricuspid regurgitation increases during inspiration.

PULMONARY HYPERTENSION

Tolazoline Test

This is done to test whether the pulmonary hypertension is reversible or not. A dose of Tolazoline is given to the patient after measuring the pulmonary arterial pressure. After giving the Tolazoline the pulmonary arterial pressure is measured. If the fall in the pulmonary pressure is more than 10 mm Hg then the pulmonary hypertension is reversible. If the fall in pulmonary arterial pressure is less than 10 mm Hg or there is no fall in the pulmonary hypertension, then the pulmonary hypertension is irreversible and the surgical closure is contraindicated.

Other agents which cause pulmonary vasodilatation are inhalation of oxygen and nitric oxide.

Grading of Pulmonary Hypertension

The radiological changes in a child with pulmonary hypertension can be classified according to the severity as follows:

- Grade I—plethora of upper part of the lung fields
- Grade II—upper and lower lung fields
- Grade III—plethora of whole lung fields
- Grade IV—peripheral pruning

Heath–Edwards Classification

The pathological changes in the small pulmonary arterioles and muscular arteries measuring <300 μm can be classified as follows:

- Type 1—changes involve medial thickening alone.
- Type 2—changes consist of medial and intimal thickening.
- Type 3—includes both plus plexiform lesions secondary to hypoplasia of the medial layer of small muscular arteries. Medial hypoplasia predisposes the arteries to aneurismal dilatation associated with severe pulmonary arterial hypertension. Plexiform lesions indicate severe, irreversible pulmonary vascular obstructive disease.

COMPLICATIONS

- Infections in the respiratory tract
- Syncope
- Arrhythmias
- Chest pain
- Haemoptysis

INVESTIGATIONS

1. Blood—polycythaemia.
2. ECG—marked RVH, right atrial dilatation and right axis deviation.
3. Chest X-ray
   - Early stage—cardiomegaly, pulmonary vascular plethora and an enlarged main pulmonary artery.
   - Advancing stage—prominent main and branch pulmonary artery with normal cardiac silhouette.
   - Late stage—normal-sized heart with diminished distal/peripheral pulmonary vascularity.
4. ECHO—left ventricular size decreased and RVH.
5. Cardiac catheterisation or colour Doppler will show increased pulmonary artery pressure and shunt between the right side and left side of the heart which may be bidirectional shunt or right-to-left shunt.
6. Arterial oxygen studies show decreased oxygen saturation.
7. Pulmonary pressure studies—pulmonary capillary wedge pressure will be normal.

8. Pulmonary vasodilators such as oxygen, nitroprusside or prostaglandins can be used to test if the shunt is reversible or irreversible.

TREATMENT

- Supportive care
- Venesections can be done with volume replacement therapy or partial exchange transfusion if polycythaemia is present.
- Single lung transplantation.
- Heart–lung transplantation.

PROGNOSIS

The prognosis is poor with the development of Eisenmenger's complex/syndrome.

CHAPTER 9

Disorders of Respiratory System

Respiratory system problems are increasing due to air pollution and increased outdoor activities by the children. The environmental history often gives a clue to the cause of respiratory infections. Any similar illness in the family should be enquired because the infection can spread easily among the family members.

HISTORY TAKING

Age

Cystic fibrosis is usually present in the newborns and infants. Foreign body aspiration is more common in children. Bronchogenic carcinoma is common in adults. Fibrosis of lungs due to tuberculosis infection is rare in children.

Gender

Smoking and its related respiratory complications are common in adolescent males.

Place

Tuberculosis infection is common in India.

Informant

The information can be given by the mother/father/guardian.

Reliability

The ranges for reliability can be good/fair/not reliable.

Presenting Complaints

These may be, for example

- Cough—since 10 days
- Fever—since 9 days
- Difficulty in breathing—since 5 days.

History of Present Illness

1. Details of the complaints should be asked in chronological order
2. Age at the onset of illness
3. Cardinal symptoms of respiratory system
    - Cough
    - Difficulty in breathing/fast breathing
    - Chest pain
    - Haemoptysis
    - Noisy breathing—wheeze or stridor
    - Other symptoms—hoarseness of voice, halitosis (lung abscess, bronchiectasis), cyanosis (occurs in severe respiratory problems due to hypoxia), haemoptysis (fresh/altered blood, frank blood/sputum stained with blood)

Some common symptoms related to the respiratory system are described further.

Cough

- Onset
- Productive or non-productive (usually the children swallow the sputum, so the mother may say that the cough is not productive)
- Character and consistency of the sputum should be noticed in older children. Consistency of the sputum may be mucopurulent in bronchitis, purulent in bronchiectasis and frothy in pulmonary oedema
- Enquiry about the foul smelling of sputum should be made. Foul smelling sputum is seen in infections with anaerobes, staphylococci, Klebsiella and Pseudomonas
- Aggravating/relieving factors
- Diurnal variation
- Seasonal variation

Fever

- High grade or low grade
- Continuous/intermittent/remittent
- Associated with chills and rigors

Chest Pain

- Site of pain
- Nature of pain
- Aggravating/relieving factors—pain of respiratory origin will get aggravated by respiratory movements such as deep inspiration
- Radiation of pain

Dyspnoea (Difficulty in Breathing)

- Onset
- Duration
- Aggravating/relieving factors
- Improving/deteriorating over a period of time

Symptoms due to Infections of the Respiratory Tract/ENT

These include sinusitis and rhinitis. The following are the common symptoms:

- Cough
- Running nose
- Ear discharge
- Ear pain
- Sore throat

Wheeze

- Inspiratory wheeze—prolonged inspiration due to larynx or tracheal obstruction, for example foreign body in the larynx or tumour of the larynx
- Expiratory wheeze—prolonged expiration due to obstruction of the bronchioles, for example bronchial asthma.

History of Past Illness

- Exanthematous fever, such as measles, predisposes to respiratory infections. Measles decreases the immunity, thus making the child vulnerable to infections of lung and the gut. Moreover, measles virus by itself causes giant cell pneumonitis, a respiratory disorder
- Whooping cough, diphtheria
- Aspiration—near-drowning, tooth extraction/dental surgery may predispose to aspiration
- Bad child-rearing practices such as instillation of oil into the nose and ears
- Change in voice (may be associated with palatal paralysis predisposing to aspiration)
- Nasal regurgitation of food or fluids
- Failure to thrive—inadequate weight gain/loss of weight
- Asthma/allergy
- Recurrent respiratory tract infections (more than six infections within the span of a single year, with each infection lasting for at least a week; these should be treated in a hospital). The number of episodes/month, severity, and whether or not they are associated with fever should be asked
- Previous hospitalisation/treatment (tapping of effusion)/surgery/anaesthesia
- In older children, rule out history of head injury, coma, convulsions, drug and poison

Antenatal History

- Booked/unbooked case
- Immunisation—two doses of tetanus toxoid (TT)
- Intrauterine infections
- Ultrasound examination done/not done in antenatal period—to rule out any congenital anomaly

Birth History

- Gestational age—full term/preterm
- Birth weight—low birth weight (LBW), small/large/appropriate for gestational age
- Mode of delivery—natural/caesarean/forceps
- Birth asphyxia—if not cried soon after the birth, then details of the resuscitation are required

Neonatal History

- Respiratory distress syndrome
- Breathing difficulty
- Feeding problems, duration of feeding
- Weight gain

Growth and Development History

Delay in growth is seen in children with chronic cough.

Nutritional History

The details of the diet of the child should be enquired.

Immunisation History

- Whether immunised/not immunised
- Details of immunisations given should be enquired
- Whether any optional vaccines given; if so, then details should be taken
- If age is less than 5 years, details of pulse polio Immunisation should be noted

Personal History

The child's likes and dislikes regarding food items should be enquired.

History of Allergy and Contact

- H/o allergy—skin, nasal, respiratory and gastrointestinal allergies, any allergy to food or drugs or presence of pets and domestic animals should be enquired.
- H/o contact with a known case of tuberculosis should be enquired.
- H/o contact with any other infectious diseases should be enquired. It is important to know if the child attends a crèche or a day-care centre as cross-infections are common in such children.

Family and Sibling History

- Consanguineous marriage
- Asthma
- Family history of hereditary diseases such as cystic fibrosis
- Diabetes mellitus
- Maternal age at conception

Socioeconomic History

- House—*pukka*/thatched
- Area of living—living area per family member
- Ventilation
- Water supply
- Per-capita income
- Overcrowding
- Hygiene
- Toilet facilities

GENERAL PHYSICAL EXAMINATION

- Level of consciousness
- Facies—in Down's syndrome, the child has typical facies. This is important because such children suffer from frequent respiratory tract infections due to immunodeficiency and hypotonia
- Nutritional status—failure to thrive is seen in long-standing lung disorders
- Decubitus—refers to the position in which the child is lying. The patients with pleural effusion prefer to lie down on the side of the effusion. This is because when the patient lies on the opposite side, the effusion compresses the opposite lung and compromises the lung volume
- Dyspnoea
- Hydration status
- Pallor
- Cyanosis—central or peripheral
- Clubbing—as seen in suppurative lung disorders

- Palmar erythema—due to polycythaemia as a result of hypoxia
- Flap—flap in hands due to carbon dioxide retention in respiratory failure
- Dental caries, oral hygiene and odour of breath
- Neck veins—engorged or not; jugular venous pressure wave patterns should be examined
- Skeletal deformities—kyphosis and scoliosis
- Signs of cardiac failure such as pedal oedema, tender hepatomegaly
- Lymph nodes—examine all nodes. Cervical nodes are commonly enlarged and matted in pulmonary tuberculosis
- Skin—examine for sinuses (tuberculous sinus), Mantoux test, BCG scar, surgical scars, focus of infection such as boils and eczema in cases of allergy

Vital Signs

- Temperature
- Pulse
- Blood pressure
- Heart rate
- Respiratory rate—Respiratory rate should be counted over 1 minute by observing the chest wall movements or the abdominal movements. Some children immediately start taking deep breaths as soon as the stethoscope is placed on the chest wall. It is better to divert the attention of the child by palpating for the pulse

Anthropometry

- Weight
- Height or length
- Midarm circumference (if the child is between 1 and 5 years of age)
- Head circumference
- Chest circumference

EXAMINATION OF RESPIRATORY SYSTEM

The examination of respiratory system consists of examination of upper respiratory tract as well as the lower respiratory tract.

Examination of Upper Respiratory Tract

The upper respiratory tract consists of the following:

- Nose
- Air sinuses
- Pharynx
- Larynx

The ear should also be examined for the presence of infections and signs of congestion.

Nose

- Anatomical defects—deviated septum, polyp
- Congestion
- Nasal discharge/rhinorrhoea
- Flaring of alae nasi
- Bleeding
- Foreign body

Air Sinuses

- Frontal sinus—tenderness at the nasion in frontal sinusitis
- Maxillary sinus—tenderness at the maxillary area in maxillary sinusitis

Pharynx

- The throat should be examined for cleft palate and postnasal drip
- Movement of the uvula
- Palatopharyngeal incoordination
- Pharyngitis
- Tonsils—enlarged, inflamed
- Adenoids—enlarged/not enlarged

Larynx

Laryngoscope should be used for examination.

Examination of Lower Respiratory Tract

Inspection

Types of Respiration. Note the type (abdominothoracic/abdominal/thoracic [Table 9.1]) and depth of respiration. See whether the respiratory movements are normal/abnormal (Table 9.2)

TABLE 9.1 Types of Respiration at Various Age Groups

Age	Type
Infant	Abdominal or diaphragmatic
Young children	Abdominothoracic
Older children after 7–8 years of age	Thoracic

TABLE 9.2 Types of Respiration According to the Part of Brain Affected

Part of Brain Affected	Type of Abnormal Respiration
Diencephalon (respiratory centre)	Cheyne stokes breathing
Midbrain	Central neurogenic hyperventilation
Upper pons	Apneustic respiration (inspiration–pause–expiration)
Lower pons	Cluster breathing
Medulla	Ataxic breathing

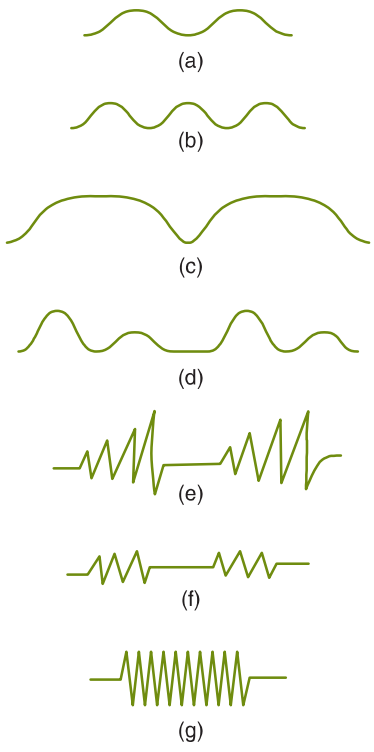


FIGURE 9.1 Types of respiration. (a) Normal rate, regular rhythm. (b) Tachypnoea—regular rhythm, rate increased for age. (c) Bradypnoea—regular rhythm, rate decreased for age. (d) Periodic breathing—irregular pattern with short periods of apnoea. (e) Cheyne stokes breathing—gradual increase in rate followed by apnoea. (f) Biot's breathing—fast and deep breathing with apnoea in between. (g) Kussmaul respiration.

(Fig. 9.1). Some abnormal types of respiration are described further.

Periodic breathing: It is an irregular pattern of breathing with periods of cessation of breathing. It is presented in newborn babies.

Cheyne stokes breathing: It is characterised by a rhythmical alteration in the depth of respiration. There is a gradual increase in rate followed by apnoea. This happens due to anoxaemia. The brain becomes less responsive to the rise in carbon dioxide level, which normally stimulates the respiratory centre. Hence, in the period of apnoea, the carbon dioxide accumulates and stimulates the respiratory centre. This results in hyperventilation and hypocapnia. This in turn leads to recurrence of apnoea. This cycle is repeated until the brain recovers. Any pathology leading to depression of the respiratory centre in the brain causes Cheyne stokes breathing.

The common causes are uraemia, intracranial tension, left ventricular failure (LVF) and poisons.

Biot's breathing: It refers to fast and deep breathing with periods of apnoea in between.

Kussmaul breathing: It is characterised by deep and rapid respiration and occurs in diabetic coma and uraemia.

Paradoxical breathing: Normally, the abdomen moves out during inspiration. In diaphragmatic paralysis, the movement occurs in the opposite direction. This leads to see-saw movements of the chest and the abdomen.

Respiratory Effort. The following findings may be present. These are suggestive of increased respiratory effort.

- Intercostal recession
- Subcostal recession
- Diaphragm—Look for paradoxical abdominal movements which are seen in diaphragmatic paralysis. Such patients cannot sniff normally
- Flaring of alae nasi
- Other accessory muscles of respiration such as sternomastoid, latissimus dorsi, pectoralis

major, serratus anterior, trapezius and abdominal muscles
- Wheeze or stridor
- Grunting—In this condition, expiration occurs with a partially closed glottis. This occurs in patients with decreased or absent pulmonary surfactant. When the alveoli collapse, the walls of the alveoli stick to each other with each respiratory cycle. The work of breathing will be enormous to release those alveoli. Hence, as an adaptive mechanism, the child maintains a positive-end expiratory pressure at the end of the expiratory phase. This causes an expiratory grunt

Examination of Chest

- Shape of the chest—symmetrical/asymmetrical
- Movements of the chest wall—symmetrical/asymmetrical. They are decreased in pleural effusion/collapse
- Deformities of the chest wall, such as pectus excavatum, barrel-shaped chest, pigeon-shaped chest and crowding of ribs
- Apical impulse
- Fullness or flattening of the intercostal spaces on the chest wall (note the areas). Fullness of the chest wall is due to trapping of air, as in asthma, which results in barrel-shaped chest

Examination of the Back

- Vertebral deformities—kyphosis or scoliosis of the vertebral column will lead to shifting of the apical impulse and restrict the lung movements
- Gibbus is seen in caries spine
- Drooping of shoulders on the side of collapse of lung. In adults, it is also seen in fibrosis
- Winging of scapula on the opposite side of collapse of lung
- Movements are symmetrical or not
- Interscapular distance should be noted

Tracheal Position

The trachea normally lies in the midline or is slightly shifted to the right side. Any cause which shifts the mediastinum will shift the trachea to that side.

Trail's sign—There is an undue prominence of the lower part (clavicular head) of the sternomastoid muscle on the side on which the trachea is shifted.

Palpation

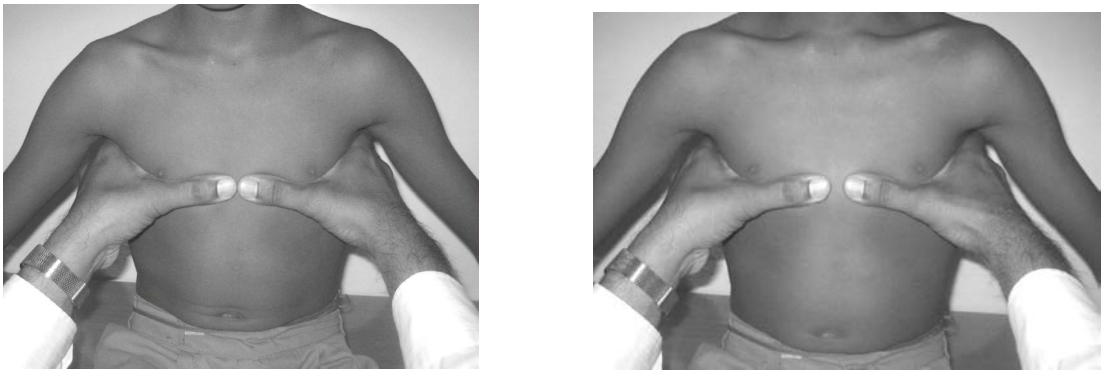
Palpation should always be done with warm hands. The findings of inspection are confirmed and better defined during palpation. The following points must be noted:

1. Position of trachea—The trachea is normally positioned centrally or is slightly shifted to the right side. The head should be fixed straight with the patient sitting or standing. The second and fourth fingers of the examining hand should be placed on each side of the sternal notch. Now with the third finger placed in the midline, the position of trachea should be assessed (Fig. 9.2a). Alternatively the tracheal position can be assessed by placing the index finger over the cricoid cartilage and sliding it downwards towards the suprasternal notch. Next, the index finger is slid in the angle between the trachea and the sternomastoid muscle. This angle will be narrowed on the side of tracheal shift and there will be resistance to the index finger (Fig. 9.2b). The side to which trachea is shifted depends on the type of lung lesion as shown in Table 9.3.
2. Chest expansion and symmetry—Chest expansion is measured by placing both the hands on either side of the chest wall. Each palm should encircle the chest wall either anteriorly or posteriorly at the level of nipples (Fig. 9.3). The thumbs should be facing each other in the midline. Note whether the thumbs move equally on the both sides. For instance, diminished movements occur on the side of pleural effusion and collapse. Measure the chest circumference in full inspiration and in full expiration. A measuring tape is used for accurate measurement of chest expansion and symmetry.
3. Chest tenderness if present should be noted.
4. Crepitus is present in pneumothorax due to subcutaneous emphysema.
5. Other palpable findings like pericardial rub, palpable rhonchi should be noted.
6. Vocal fremitus—It is the vibration detected by palpating the chest with the palm of the hand placed flat on the chest wall. The patient is asked to repeat some common words such as 'one, one, one' and the palm is placed on the chest wall.



(a) (b)

FIGURE 9.2 Method of palpation of trachea.



(a) (b)

FIGURE 9.3 Method of eliciting chest expansion from front. Note the movement of thumbs during inspiration and expiration.

TABLE 9.3 Respiratory Conditions Associated with or without Tracheal Shift

Opposite Side of Lesion	Same Side of Lesion	No Shift
Pleural effusion	Collapse	Consolidation
Empyema	Fibrosis	Emphysema
Hydropneumothorax		Bronchiectasis
Pneumothorax		Bronchial asthma

Vibrations are felt by the palpating hand. This is known as vocal fremitus. It must be noted whether the vocal fremitus is normal, decreased or increased (Table 9.4). Always compare the tactile fremitus on the contralateral side with the corresponding site. For instance, if the right infraclavicular region is being examined, it should be compared with the left infraclavicular region.

TABLE 9.4 Vocal Fremitus

Increased	Diminished	Absent
Consolidation Large superficial cavity	Bronchial obstruction	Pleural effusion Pneumothorax Collapse Fibrosis

Percussion

The examination of the respiratory system is usually done anteriorly in the midclavicular line, laterally in the mid axillary line and posteriorly in the scapular line.

Direct Percussion. Tap the part, like clavicle, directly with one finger. This method is used for percussion of lung apices.

Conventional Percussion. The chest wall is percussed and findings of percussion are noted (Fig. 9.4). The presence of pain and tenderness during percussion should also be noted. The percussion note is altered in various conditions (Table 9.5).

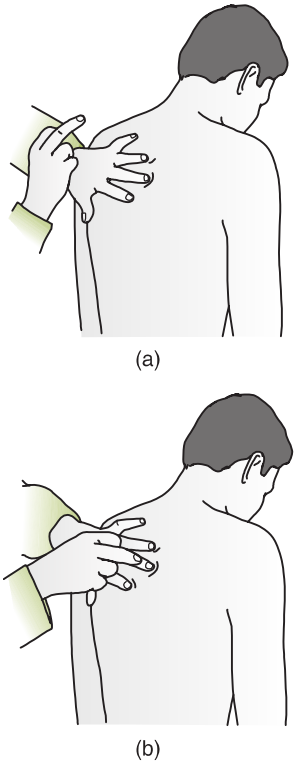


FIGURE 9.4 Methods of percussion.

TABLE 9.5 Percussion Findings in Various Respiratory Disorders

Percussion Note	Respiratory Condition
Hyper-resonant	Pneumothorax
Resonant	Normal
Impaired/dull	Consolidation Collapse Thickened pleura Fibrosis Abscess Fibrosis (rare in children) Infarction of lung Sequestration of lung
Stony dull	Pleural effusion Massive collapse consolidation Solid tumours

Areas of Percussion. The percussion findings on one side should always be compared immediately with the corresponding findings on the contralateral side. For example, when the right infraclavicular region is percussed, the left infraclavicular region for comparison should also be percussed before proceeding to a different site. The areas to be percussed on the chest wall bilaterally are as follows:

1. Direct percussion
   - Clavicle
2. Indirect percussion
   - Kronig's isthmus
   - Supraclavicular
   - Infraclavicular
   - Inframammary
   - Axillary
   - Infra-axillary
   - Suprascapular
   - Interscapular
   - Infrascapular

Percussion for Shifting Dullness. This is positive in hydropneumothorax. Percuss the chest with the child sitting and note for dullness on the side of the hydropneumothorax. When dullness is noted, ask the patient to lie down on the opposite side and percuss after a few seconds. For example, in

right-sided hydropneumothorax, percuss for dullness with the child in sitting position. Now, ask the child to lie down in the left lateral position. Percuss again after few seconds. If the area becomes resonant, shifting dullness is present.

Coin Test. Place a coin on the anterior chest wall and tap it with another coin. Auscultate from the corresponding opposite side of the back. A typical high pitched bell-like metallic sound is heard in patients with tense pneumothorax and hydropneumothorax.

Tidal Percussion. It is done to differentiate whether the dullness on the right side is due to pleural effusion or due to hepatomegaly. The anterior wall of the chest is percussed from the right second intercostal space along the midclavicular line. Once the dullness is noted in the inferior part with the percussing finger in position, the patient is asked to take a deep breath. Again the same spot is percussed. If the dullness is due to pleural effusion, it will persist; and if the dullness is due to liver, the area becomes resonant (as the liver will be pushed down by the expanding lung).

Cardiac Dullness. The area of cardiac dullness may be decreased in emphysema due to the overlapping lung.

Traube's Space. This space is bounded medially by the left lobe of liver, laterally by spleen, above by the left dome of diaphragm and below by the left costal margin (Fig. 9.5). It overlies the fundus of the stomach. Hence, it is normally tympanitic on percussion. It becomes dull in the following conditions:

- Left-sided pleural effusion
- Hepatomegaly (left lobe)
- Splenomegaly
- Situs inversus totalis (in this condition, this space is present on the right side)

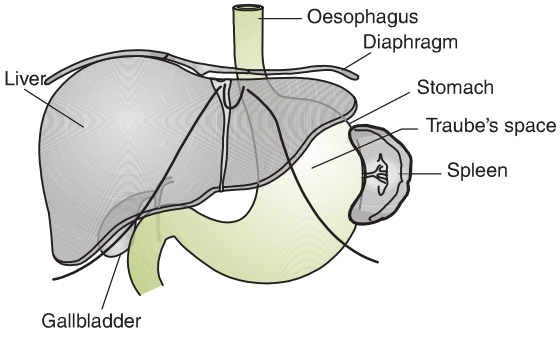


FIGURE 9.5 Traube's space.

Auscultation

The following areas are auscultated in a systematic manner on both sides:

- Supraclavicular
- Infraclavicular
- Inframammary
- Axillary
- Infra-axillary
- Suprascapular
- Interscapular
- Infrascapular

The following should be noted in auscultation of the above areas.

Breath Sounds

- Present or absent (Table 9.6)
- Intensity—normal/increased/decreased
- Quality of the breath sounds—vesicular/ bronchial (Fig. 9.6, also see Table 9.7)

Vocal Resonance. It is the resonance perceived by the examiner during auscultation of the chest while the child is repeating words like 'one, one, one' (Table 9.8). Note the intensity and character of vocal resonance. Intensity depends upon the following factors:

TABLE 9.6 Pathophysiology of Absent Breath Sounds

Part of Respiratory Tract	Causes
Absence of lung	Agenesis Pneumonectomy
Pleura	Pleural thickening Pleural effusion Pneumothorax
Alveoli	Collapse
Airway obstruction	Foreign body—total obstruction of the bronchus Severe asthma

TABLE 9.7 Types of Breath Sounds

Types of Breath Sounds	Character		Pitch	Respiratory Conditions
Vesicular	Inspiration more than the expiration No pause		Low pitched	Normal
Bronchial	Inspiration equal to expiration with a pause present	Tubular	High pitched	Consolidation, collapsed lung with patent bronchus
		Cavernous	Low pitched	Thick-walled cavity with connection with bronchus
		Amphoric	Low pitched, metallic quality	Tension pneumothorax, bronchopleural fistula
Bronchovesicular breathing	Expiration more than the inspiration with no pause in between		High/low pitched	Bronchial asthma, emphysema

- Loudness of patient's voice
- Depth of voice
- Conductivity of lungs
- The distance between the bronchus and the stethoscope

Types of vocal resonance according to the character are as follows:

1. *Bronchophony:* Vocal resonance of normal intensity gives an impression as if it is produced in the chest piece of the stethoscope. In bronchophony, it appears to be originating near the earpiece. It is heard over an area of consolidation.
2. *Whispering pectoriloquy:* The patient is asked to whisper some words such as one, two and three. The words are heard distinctly as if spoken into the ears. This is seen in consolidation, and if there is a large cavity communicating with a bronchus or large bronchus surrounded by solid lung. This can also be heard in the adjacent areas lying near trachea or large bronchi.
3. *Aegophony:* It is the nasal or bleating quality of the vocal resonance heard over an area of consolidation or just above the area of pleural effusion. It is due to the dilatation of the lungs at this site and the compression of the lungs from below.

TABLE 9.8 Variation of Intensity of Vocal Resonance in Different Respiratory Conditions

Vocal Resonance	Respiratory Conditions
Increased	Consolidation Superficial cavity
Decreased	Collapse Fibrosis
Absent	Pleural effusion Pneumothorax Empyema Hydropneumothorax Emphysema Bronchial obstruction

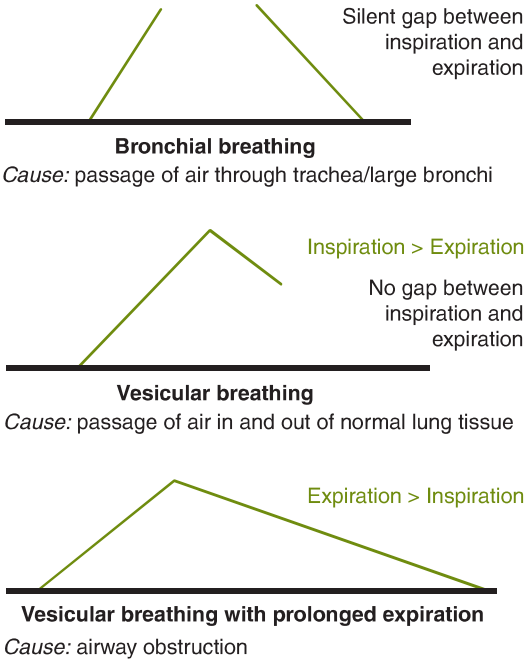


FIGURE 9.6 Breath sounds.

Adventitious Sounds

1. *Wheezes (rhonchi)* are continuous prolonged musical sounds which arise in the bronchi. They may be high pitched (when a large lumen is obstructed as in bronchitis and asthma); or low pitched (when a small lumen is obstructed as in bronchiolitis).

   Wheeze is initially heard during expiration, but when the obstruction is severe, it may also be heard during inspiration, as occurs in severe bronchial asthma. Rhonchi are heard in cases of bronchitis, bronchial asthma, foreign body obstruction, bronchiolitis and left ventricular failure.
2. *Crepitations* (fine/coarse) are discontinuous crackling or bubbling sounds of short duration (Table 9.9).
3. *Pleural friction rub* is heard in pleurisy. It is due to rubbing of both the layers of pleura against each other during respiration. The rub will be heard when there is an inflammation of pleura or there is not enough fluid in the pleural cavity separating both the parietal and visceral pleura. Pleural friction rub is associated with the respiratory movements and is heard during both inspiration and expiration. It will be decreased on pressing the chest with the auscultation stethoscope. This is because the compression results in decreased chest movements. The rub is not heard if the patient holds his breath.
4. *Stridor* is a harsh noise heard during respiration. It may be inspiratory or expiratory. It may be aggravated by coughing. It is caused by partial obstruction to the bronchus by a foreign body or mass.

TABLE 9.9 Differentiating Features between Fine and Coarse Crepitations

Features	Fine Crepitations	Coarse Crepitations
Pathogenesis	Presence of fluid in the alveoli	Secretion of fluid in the bronchi or sudden opening of stiff alveoli
Conditions	Left-ventricular failure Early stage of consolidation Fibrosis	Bronchiectasis Late stage of consolidation Lung abscess

Other Findings

- Succussion splash—the chest wall is auscultated by shaking the patient. The presence of fluid in hydropneumothorax causes a splash and can be auscultated.
- Post-tussive suction—in presence of a cavity, immediately after cough, air will be sucked into the cavity. This sound is heard by auscultation.

INVESTIGATIONS

1. Blood haemogram with ESR
   - Total count—leucocytosis in bacterial infections
   - Differential count—lymphocytosis in tuberculosis
   - Haemoglobin (%)
   - Erythrocyte sedimentation rate
2. X-ray chest
   - Right-upper lobe pneumonia may be due to aspiration
   - Right-middle lobe pneumonia may be due to bronchial obstruction
   - Multiple small abscesses may be suggestive of infection due to Staphylococcus or Klebsiella
   - Acute lobar pneumonia may be pneumococcal in origin
3. Investigations to find out the causative agents or organisms
   - Throat swab examination
   - Nasopharyngeal aspirate examination
   - Sputum examination
   - Gastric lavage examination
4. Mantoux test/accelerated BCG reaction (to rule out pulmonary tuberculosis)
5. Ultrasonography
6. Thoracocentesis (pleural tap)
7. Endoscopic studies—fiberoptic bronchoscopy with bronchoalveolar lavage (BAL)
8. CT scan if needed
9. Lung function tests (help to assess the severity and the improvement)
   - Tidal volume (TV)—the volume of air either inspired or expired during tidal respiration

- Inspiratory reserve volume (IRV)—the volume of air that enters the lungs by forcible inspiration after tidal inspiration
- Expiratory reserve volume (ERV)—the volume of air expired by forcible expiration after tidal expiration
- Residual volume (RV)—the volume of air remaining within the lungs at the end of maximal expiration
- Total lung capacity (TLC)—air contained within the lungs after a maximal inspiration
- Inspiratory capacity (IC)—the volume of air inspired by deep inspiration
- Forced vital capacity (FVC)—denotes the quantity of air expired forcefully after maximal inspiration
- Functional residual capacity (FRC)—the volume of air remaining in the lungs at the end of normal expiration
- Peak expiratory flow rate is reduced in obstructive airway disorders such as asthma

10. Miscellaneous
    - Sweat chloride test for cystic fibrosis
    - Evaluate for gastro-oesophageal reflex (oesophageal pH, radionucleotide scans) in a case of recurrent/persistent pneumonia
    - Evaluate for swallowing (barium swallow will show palatopharyngeal incoordination which will cause aspiration of feeds)

PNEUMONIA

Pneumonia is an inflammatory process which involves the lung parenchyma.

PATHOGENESIS

Pneumonia results from

- Aspiration
- Contiguous spread of virulent agents from upper airways
- Secondary infection when there is disruption of protective mechanism
- Haematogenous spread

CLASSIFICATION

Anatomical Classification

1. *Lobar or lobular pneumonia*—characterised by replacement of alveolar air with cellular exudates.
2. *Interstitial pneumonia*—characterised by massive proliferation and desquamation of alveolar cells.
3. *Bronchopneumonia*—characterised by spreading inflammation of the terminal bronchioles.
4. *Multilobar pneumonia.*

Based on the Duration of Symptoms

1. *Persistent pneumonia*—persistence of symptoms and X-ray abnormalities for more than 4 weeks.
2. *Recurrent pneumonia*—two episodes of pneumonia in 1 year or more than three episodes at any time with X-ray clearance between two episodes of illness.

Based on the Aetiological Factors

1. *Infective*—Pneumonia occurs as a result of invasion of lungs due to microorganisms such as bacteria and viruses as given in Table 9.10. The differences between bacterial and viral pneumonia are summarised in Table 9.11.
2. *Non-infective*—chemical.

Based on the Immunity

1. *Primary pneumonia*—it is caused by organisms of high virulence and as such, it even affects those with good immunity.
2. *Secondary pneumonia*—this occurs with organisms of low virulence. Either the immunity of the host is diminished or some predisposing factor is present such as aspiration.

Based on the Source of Infections

1. *Community acquired pneumonia* is caused by organisms present in the community in children

TABLE 9.10 Causative Organisms in Pneumonia

Infective Pneumonia	Aetiological Agents
Bacterial pneumonia	*Streptococcus pneumoniae* *H. influenzae* *Staphylococcus aureus* *Mycobacterium tuberculosis* *Pseudomonas aeruginosa*
Atypical pneumonia	*Chlamydia* *Mycoplasma* *Legionella*
Viral pneumonia	Respiratory syncytial virus Parainfluenza virus Influenza virus Rhinovirus Adenovirus

TABLE 9.11 Differences between Bacterial and Viral Pneumonia

Features	Bacterial Pneumonia	Viral Pneumonia
Onset	Abrupt	Gradual
Epidemic	Not seen	Common
Associated conditions	Infection at other sites, septicaemia	Associated with URI, coryza
Fever	High grade	May be absent
Toxemia	Common	Absent
Respiratory distress	Common	Common in infants
Lung signs	Crackles ++	Wheeze ++
X-ray chest	Confluent infiltrates	Diffuse in peripheral areas
Pleural involvement	May be seen	Not common
Prognosis	Complications such as empyema, pneumatocele, septicaemia may be seen	Self-limiting, usually resolves in about a week. Hyperinflation seen in respiratory syncytial virus (RSV) infection

who have not been hospitalised in the recent past.

2. *Hospital acquired pneumonia* is caused by organisms present in the hospital. It occurs after at least 48–72 hours of being admitted in the hospital.
3. *Opportunistic pneumonia* is seen in children with decreased immunity and is caused by organisms which usually do not cause pneumonia (Table 9.12).

TABLE 9.12 Causative Agents in Various Types of Pneumonia

Type of Pneumonia	Causative Agent
Community acquired pneumonia	
• Typical	*S. pneumoniae* *H. influenzae* *S. aureus*
• Atypical	*Mycoplasma* *Chlamydia* *Legionella*
Hospital acquired pneumonia	*E. coli* *Proteus* *Klebsiella* *S. aureus* *Pseudomonas*
Opportunistic pneumonia	*P. carinii* Cytomegalovirus (CMV) Varicella zoster

AETIOLOGY

The causative organism depends on the following factors:

- Age (Table 9.13)

TABLE 9.13 Common Organisms Causing Pneumonia in Various Age Groups

Organisms	Neonates	1 month to 5 years	Above 5 years
Bacteria	Group B streptococci *E. coli* *Klebsiella* *Listeria* *S. aureus*	*S. pneumoniae* *S. aureus* *H. influenzae* Group A *Streptococcus* *Klebsiella* *Pseudomonas* *M. tuberculosis*	*S. pneumoniae* *S. aureus* *H. influenzae* *M. tuberculosis*
Viruses	CMV Herpes	CMV RSV Influenza virus Adenovirus	Influenza virus Varicella
Atypical organisms	Chlamydia	Mycoplasma	Mycoplasma Legionella Chlamydia

TABLE 9.14 Common Organisms Causing Pneumonia in Immunocompromised Children

Protozoa	Bacteria	Viral	Fungal
P. carinii	Gram positive • *S. pneumoniae* • *S. aureus*	CMV Varicella zoster Measles giant cell pneumonia	Candidiasis Aspergillus
	Gram negative • *Klebsiella* • *Pseudomonas* • *H. influenzae* • *Legionella*	RSV Herpes simplex HIV	

- Congenital anomalies such as cleft palate and tracheo-oesophageal fistula predispose to aspiration pneumonia by organisms present in the oral cavity.
- Immunity status—Klebsiella infection is common in immunocompromised children (Table 9.14).
- Underlying lung disease—*S. aureus, H. influenzae* and *P. aeruginosa* are the three most common organisms causing lung infections in cystic fibrosis patients.
- H/o exposure to infection—when one of the family members is infected with an organism, the possibility of the same infection in other child becomes more.

PREDISPOSING FACTORS

Host Factors

1. Age—below 6 months
2. Neonatal factors—preterms and babies with low birth weight
3. Congenital defects (may predispose to aspiration)—cleft palate, tracheo-oesophageal fistula, ciliary dyskinesia, sequestration and cysts of lungs
4. Bad child-rearing practices—bottle feeding, lack of breastfeeding
5. Nutritional factors—protein energy malnutrition, vitamin A deficiency (severe), iron deficiency anaemia, zinc deficiency and so on
6. Systemic factors
   - Cardiovascular causes—congenital heart diseases, left to right shunts
   - Gastrointestinal causes—cricopharyngeal incoordination, gastro-oesophageal reflux
   - Chronic lung diseases—asthma, cystic fibrosis
   - Others—measles, diarrhoea, sinusitis, otitis media
7. Immunological status—immunosuppressed states
8. Malignancy
9. Iatrogenic—anaesthesia
10. Trauma

Environmental Factors

- Overcrowding
- Number of siblings (order of birth)
- Indoor air pollution
- Sanitation
- Passive smoking
- Educational status

CLINICAL FEATURES

Symptoms

- Fever
- Fast and difficult breathing
- Cough
- Chest pain
- Abdominal pain
- Poor feeding
- Irritability
- Excessive sleepiness

Signs

- Tachypnoea
- Chest retraction
- Grunting and stridor
- Nasal flaring
- Cyanosis
- Dullness on percussion
- Diminished breath sounds, wheeze and crackles on auscultation
- May be associated with meningismus, paralytic ileus

- Right lower lobe pneumonia causes diaphragmatic irritation which may present as hiccoughs

INVESTIGATIONS

1. Chest radiography—posteroanterior and lateral films. Salient radiological findings in various types of pneumonia are listed in Table 9.15.
2. Total and differential blood count, haemoglobin
3. Tests to identify organisms
   - Microscopic examination—gram staining and acid fast bacteria (AFB) staining
   - Serological tests for bacteria and viruses
   - Urinary antigen tests for bacterial antigens and viral antigens
   - Rapid antigen detection tests such as direct fluorescent antibody test
   - Polymerase chain reaction for Mycobacterium
   - Culture studies in sputum and blood

Specimens to identify the organisms are taken from nasopharyngeal aspirate, throat swab, bronchoalveolar lavage and lung aspirates.

INDICATIONS FOR ADMISSION

- Severe malnutrition
- Immunodeficiency
- Severe anaemia
- Disseminated infection, septicaemia and shock
- Drowsiness and altered sensorium
- Decreased oxygen saturation (PaO_2 < 80 mm Hg at room air)
- Leucopenia (<4000/mm^3) or leucocytosis (≥30,000/mm^3)
- Culture and sensitivity results—growth of *Staphylococcus aureus*

TABLE 9.15 Radiological Findings in Various Types of Pneumonia

Radiological Changes	Type of Pneumonia
Lobar involvement	Pneumococcal pneumonia
Right middle lobe pneumonia	Aspiration pneumonia
Upper lobe pneumonia, cavitations, bronchopneumonia with hilar lymphadenopathy	Tuberculous pneumonia
Lower lobe pneumonia	Chemical pneumonitis
Multiple abscesses	Staphylococcal/Klebsiella pneumonia
Bilateral interstitial pneumonia	Viral pneumonia
Bilateral interstitial pneumonia in immunosuppressed children	*Pneumocystis carinii* pneumonia

TREATMENT

Clinical classification and management of pneumonia as per ARI control programme is discussed on page 412. Antimicrobial therapy for specific agents is discussed next.

Antimicrobial Therapy

Community Acquired Pneumonia

Infective agents	Drugs	Dosage
Neonates		
Group B Streptococci, *Escherichia coli*	Ampicillin + gentamycin	100 mg/kg/day 3–5 mg/kg/day
S. aureus	Cloxacillin + gentamycin	100 mg/kg/day 3–5 mg/kg/day
Infants (1 month–1 year)		
Group B Streptococci	Ampicillin + gentamycin	100 mg/kg/day 3–5 mg/kg/day
S. aureus	Cloxacillin + gentamycin	100 mg/kg/day 3–5 mg/kg/day
H. Influenzae type B	Penicillin/ ampicillin	1 lakh units /kg/day 100 mg/kg/day
S. pneumoniae	Penicillin	1 lakh units/kg/day for 2–3 weeks
Chlamydia	Erythromycin	40 mg/kg/day
Children older than 1 year		
S. pneumoniae	Penicillin/ ampicillin Cefotaxime	50,000–1,00,000 units/kg/day 100 mg/kg/day 100 mg/kg/day

Infective agents	Drugs	Dosage
Anaerobes	High dose penicillin + metronidazole	1 lakh units/kg/day
H. Influenzae	Ampicillin Ceftriaxone Cefuroxime	100 mg/kg/day 50–75 mg/kg/day 50–100 mg/kg/day
Atypical pneumonia		
• *Legionella*	Erythromycin	40 mg/kg/day
• *Mycoplasma*	Erythromycin	40 mg/kg/day
• *Chlamydia*	Erythromycin, Co-trimoxazole	40 mg/kg/day Trimethoprim: 20 mg/kg/day and sulfamethoxazole: 100 mg/kg/day
Viral pneumonia		
• Influenza A	Amantadine	Amantadine: 4.4–8.8 mg/kg /24 hour for children 1–9 years of age (maximum dose 150 mg/day), 200 mg/24 hour for children >9 years of age
• Influenza A and B	Zanamivir Oseltamivir	Oseltamivir: 30 mg twice a day for children who weigh ≤15 kg, 45 mg twice a day for children who weigh >15–23 kg, 60 mg twice a day for those who weigh >23–40 kg and 75 mg twice a day for those who weigh >40 kg
• RSV	Ribavirin	Aerosol for 12–18 hours for 3–7 days
• Herpes	Acyclovir	10 mg/kg/dose for 10 days

Hospital Acquired Pneumonia

Organism	Treatment
S. aureus	Cloxacillin: 100–200 mg/kg in 3–6 divided doses Methicillin: 100–200 mg/kg in 3–6 divided doses Vancomycin: 40 mg/kg in 3–6 divided doses
P. aeruginosa	Ceftazidime: 100–150 40 mg/kg/day Carbenicilin: 200–400 mg/kg/day + gentamycin 3–5 mg/kg/day Tobramycin: 3–5 mg/kg/day + amikacin 15–25 mg/kg/day
Anaerobes	Metronidazole, clindamycin
Gram-negative organisms	
H. influenzae	Ampicillin: 100 mg/kg/day + chloramphenicol 100 mg/kg/day or ceftriaxone 100 mg/kg/day for 10–14 days
E. coli, Klebsiella	Aminoglycosides

Opportunistic Pneumonia

Organism	Treatment
Pneumocystis carinii	Co-trimoxazole Trimethoprim: 20 mg /kg/day and sulfamethoxazole 100 mg/kg/day

Supportive Treatment

- Oxygen
- Intravenous fluids (plenty of oral fluids, if the child is able to drink)
- Good nutrition
- If fever is present then tepid sponging should be given. Paracetamol will also be helpful
- Predisposing factors should be avoided
- Physiotherapy

PREVENTION

- Immunisation
- Health education to the mother (avoid bad child-rearing practices such as oil instillation)
- Proper implementation of ARI control programme
- High risk factors should be avoided

RECURRENT AND PERSISTENT PNEUMONIA

If there are two episodes of pneumonia in a year or more than three episodes at any time with X-ray clearance between two episodes of illness it is considered as recurrent pneumonia.

Persistent pneumonia is characterised by symptoms and X-ray abnormalities of more than 4 weeks.

Aetiology

- Congenital
- Acquired

These are discussed in Table 9.16.

TABLE 9.16 Aetiology of Recurrent and Persistent Pneumonia

Causes	Conditions
Congenital	
Infectious	Cytomegalovirus
Non-infectious	Congenital defects like cleft palate
	Tracheo-oesophageal fistula
	Gastro-oesophagal refux
	Sequestration of lung
	Defect in clearance—cystic fibrosis/defective mucociliary functions
	Immunodeficiency (*P. carinii*, fungal infections, *Legionella*)
	Haemosiderosis
	Sickle cell anaemia
Acquired	
Infectious	Otitis media, sinusitis, bronchiectasis, pulmonary tuberculosis, cytomegalovirus infection and chlamydial infection
Non-infectious	Recurrent aspiration
	Foreign body aspiration
	Asthma
	Loeffler's pneumonia
	Interstitial lung disease

ATYPICAL PNEUMONIA

It is also known as 'walking pneumonia'. The children with these infections present with atypical symptoms. Differences between atypical pneumonia and typical pneumonia are shown in Table 9.17. The common types of atypical pneumonia are

- Mycoplasma pneumonia
- Chlamydia pneumonia
- Legionella pneumonia

TABLE 9.17 Differences between Typical Pneumonia and Atypical Pneumonia

Features	Typical Pneumonia	Atypical Pneumonia (Walking Pneumonia)
Causative organisms	*S. pneumoniae* *H. influenzae* *S. aureus*	*M. pneumoniae* *Chlamydia pneumoniae* *Legionella*
Onset	Sudden	Gradual
Age	Any age	Usually >5 years, except Chlamydia which commonly occurs within the first 6 months
Fever	Common	May be present
Cough	Productive	Dry
Symptoms	Pulmonary	Systemic
X-ray chest findings	Localised	Diffuse

Mycoplasma Pneumonia

The causative organism is *Mycoplasma pneumoniae*. This may present as mild upper respiratory tract infection, bronchitis, bronchiolitis or bronchopneumonia. This causes a benign self-limiting illness.

Clinical Features

It starts with influenza-like syndrome with fever, malaise, headache, sore throat and cough. Symptoms will be more than the signs. Temperature rarely exceeds 38.5°C. The common clinical features are as follows:

- Influenza-like syndrome
- Skin rashes
- Arthralgia
- Haemolytic anaemia
- Muscle tenderness
- CNS—features suggestive of aseptic meningitis, cerebellar ataxia, transverse myelitis, Gullian–Barre syndrome
- Chest—crepitations, localised wheeze, dullness due to atelectasis or fluid collection

Investigations

1. X-ray findings
   - Varied bronchopneumonic infiltrates in the lower lobes
   - Small areas of segmental or subsegmental atelectasis
2. Serological tests
   - IgM antibodies

Chlamydia Pneumonia

The causative organism is *Chlamydia trachomatis* which usually causes infection in the first 6 months of life. The source of infection is infected birth canal. It occurs between 3 weeks and 3 months of life

Clinical Features

- Nasal obstruction
- Cough
- Tachypnoea
- Absence of fever
- Conjunctivitis
- Secretary otitis media

Investigations

- X ray—symmetrical involvement with interstitial type infiltrates and patches of airless lung
- Culture of organism from nasopharyngeal secretions
- Immunoflourescence, ELISA

Legionella Pneumonia

Clinical Features

1. Mild cough, malaise, fatigue and anorexia
2. Extrapulmonary manifestations are common in immunosuppressed patients.
   - Renal failure
   - Carditis—myocarditis, pericarditis, endocarditis
   - Peritonitis
   - Cellulitis
   - Pancreatitis
   - Pyelonephritis

Investigations

- Culture of respiratory secretions
- Antigen detection by ELISA

Treatment of Atypical Pneumonia

Macrolides are used for treatment of atypical pneumonia. These are as follows:

- Erythromycin—40 mg/kg/24 hour in four divided doses
- Roxithromycin—5 mg/kg/24 hour
- Azithromycin—10 mg/kg/24 hours. It has an advantage of once a day dose and shorter duration of therapy. It has better penetration and bioavailability
- Clarithromycin—15 mg/kg/24 hour

PREVENTION OF RESPIRATORY INFECTIONS

The following methods are used to control and prevent acute respiratory infections in children.

- Acute respiratory infections (ARIs) control programme
- Treatment of children with pneumonia
- Teaching the mothers and health care/paramedical workers about the recognition of fast breathing, chest indrawing and danger signs of pneumonia
- Administration of vitamin A to all children aged 0–5 years
- Promotion of exclusive breastfeeding

Acute Respiratory Infections Control Programme

ARIs are one of the major causes of increased morbidity and mortality in children under the age of 5 years. Hence, the World Health Organization had devised certain guidelines for early diagnosis and treatment of respiratory infections. The following two criteria are taken as suggestive of respiratory infection:

- Cough
- Difficulty in breathing

TABLE 9.18 Classification and Treatment in ARI Programme in the Age Group of 2 months–5 years

Classification	Clinical Features	Treatment	Place
No pneumonia	Cough No fast breathing No chest indrawing Feeding well	Treat like URI. No antibiotics Ask the mother to observe for increased respiratory rate or chest indrawing. Treat underlying condition. Treat fever and wheezing, if present	Home
Pneumonia	Cough No chest indrawing Able to drink Fast breathing	Co trimoxazole orally 5–8 mg/kg of trimethoprim 25 mg/kg of sulfamethoxazole Treat fever and wheezing, if present	Home/health care centre Reassess after two days and manage accordingly
Severe pneumonia	Lower chest indrawing present Able to drink Fast breathing ± Other signs may be present—nasal flaring, grunting, cyanosis	Antibiotics: Ampicillin + gentamycin or Penicillin 25,000 units /kg/dose every 6 hours or Cefotaxime or ceftriaxone + gentamycin for 14 days Oxygen	Admit in hospital Assess once daily
Very severe pneumonia	Not able to drink Cyanosis Stridor in calm child Severe respiratory distress (head nodding) or grunting Lethargy/excessive drowsiness Convulsions	Antibiotics: cefotaxime or ceftriaxone + gentamycin for 14 days Oxygen	Admit in hospital Assess twice daily

Note: If severe malnutrition is present, the child should be treated as a case of very severe pneumonia. Children below 2 months of age will be more prone to develop serious course. They should be treated with parentral antibiotics. A combination of ampicillin and gentamycin can be given for 7–10 days.

Fever is not taken as an essential criterion for respiratory infection. Fast breathing is the most sensitive sign to identify pneumonia in the community. Classification and treatment according to ARI programme is given in Tables 9.18–9.20.

TABLE 9.19 Treatment of Pneumonia: Dose Schedule of Cotrimoxazole

Age	Weight (kg)	Tablet:Trimethoprim 20 mg and Sulfamethoxazole 100 mg
<2 months	3–4	1 tablet twice daily
2–12 months	6–9	2 tablets twice daily
1–5 years	10–19	3 tablets twice daily

TABLE 9.20 Treatment of Severe Pneumonia

Drug	Dosage	Interval
Benzyl penicillin	50,000 IU/kg/dose	Every 6 hours
Ampicillin	50 mg/kg/dose	Every 6 hours
Chloramphenicol	25 mg/kg/dose	Every 6 hours

Danger Signs in Respiratory Infection

- Apnoea
- Audible wheeze
- Breathing difficulty—severe respiratory distress (head nodding) or grunting
- Central cyanosis
- Dyspnoea
- Excessive drowsiness/lethargy
- Flaring of nose
- Grunting
- Hypothermia
- Inability to drink or take food
- Indrawing of chest
- Stridor at rest
- Severe malnutrition

Indications for X-ray

In most of the cases X-ray is not needed. However, X-ray should be taken when any of the following are present:

- Staphylococcal infection

- No improvement with treatment
- Effusion
- Pneumothorax
- Severe pneumonia and very severe pneumonia
- H/o foreign body aspiration
- Persistent cough for more than 30 days
- To exclude other conditions such as cardiac failure
- Pneumonia associated with features of septicaemia

COMPLICATIONS

Pneumonia can cause lot of complications in untreated cases as well as in some treated cases. These are summarised in Table 9.21.

TABLE 9.21 Complications of Pneumonia

System	Complications
Respiratory	
Pulmonary	Suppurative lung diseases such as lung abscess (following staphylococcal and Klebsiella infections)
	Collapse
	Bronchiectasis
Pleural	Parapneumonic effusion
	Empyema
	Pneumothorax (following staphylococcal infections)
	Pyopneumothorax
Cardiovascular	Acute circulatory failure due to bacteraemia
	Pericarditis
	Endocarditis
Miscellaneous	Meningism
	Shock due to bacteraemia
	Multiorgan failure

PULMONARY CONSOLIDATION

Pulmonary consolidation is defined as exudative solidification of lung parenchyma due to an inflammatory pathology.

AETIOLOGY

1. Infections
   - Bacterial
   - Viral
   - Rickettsial
   - Mycotic
   - Protozoal
   - Fungal
   - Spirochaetal
2. Collagen diseases
   - SLE
   - Rheumatoid arthritis
   - Polyarteritis
3. Aspiration
4. Toxic agents—gas and smoke
5. Occupational

CLINICAL FEATURES

History

- Cough (productive/non-productive)
- Fever
- Malaise
- Breathlessness
- Pain in the chest

General Examination

- Conscious state
- Appearance of the child—ill looking (toxic looking)/anxious looking
- Cyanosis
- Dyspnoea

Vital Signs

- Tachycardia
- Tachypnoea
- Temperature—elevated

Respiratory System Examination

1. Inspection findings
   - Tracheal site—normal (will not be shifted)
   - Apical impulse at normal site
   - Diminished movements of the chest on the involved side
   - Fullness/flatness of the chest wall (areas should be noted)

- Check for involvement of accessory muscles of respiration, look for signs like intercostal recession, subcostal recession, flaring of alae nasi

2. Palpation findings
   - Inspection findings are confirmed
   - Restricted movements on the affected area
   - Tactile fremitus increased
   - Vocal fremitus increased
3. Percussion findings—Impaired note on percussion over the areas of consolidation
4. Auscultation findings
   - Bronchial breath sounds
   - Vocal resonance—increased
   - Bronchophony
   - Whispering pectoriloquy—the words whispered are heard clearly when auscultated over the area of consolidation. This is because the fluid in the alveoli acts as the interface between the sounds in the bronchus and the chest wall. (Normally air in the alveoli acts as the interface.) The fluid conducts the sounds better than air, hence sounds are heard clearly
   - Crepitations are more in resolving consolidation
   - Rhonchi may be present due to oedema of the bronchioles, which are relatively small in children as compared to adults
   - Pleural rub may be present if associated with pleuritis

INVESTIGATIONS AND TREATMENT

The following investigations are done in a case of pulmonary consolidation:

- Total blood count
- Differential blood count
- X-Ray chest—homogenous opacification of the involved part (Fig. 9.7)
- Mantoux test—to rule out tuberculosis
- CT scan may be helpful to confirm the diagnosis

It should be treated with appropriate antibiotics according to the aetiology.



FIGURE 9.7 X-ray chest showing consolidation of right upper lobe.

PLEURAL EFFUSION

Pleural effusion is defined as an abnormal accumulation of fluid in the pleural space, that is, the space between the parietal and visceral pleura.

PATHOGENESIS

Fluid accumulates in the pleural cavity due to either altered hydrostatic and oncotic pressures or altered permeability of the pleura. When pleural effusion is due to systemic factors which alter the hydrostatic or oncotic pressures and there is no change in the pleural permeability, it is called a transudative effusion.

When pleural effusion is due to the factors which alter the permeability of pleural membranes, it is known as exudative effusion.

The following factors have a role in the development of pleural effusion:

- Altered permeability of the pleural membranes
- Increased capillary permeability due to inflammation or trauma, hypersensitivity, uraemia, pancreatitis and malignancy
- Increased capillary hydrostatic pressure in the systemic circulation or pulmonary circulation
- Decreased oncotic pressure in the vessels
- Impaired lymphatic drainage due to blockage or rupture of thoracic duct

- Persistent increase in pleural fluid oncotic pressure, causes more accumulation of fluid

Pleural Effusion in a Child with Ascites

The following causes predispose to the development of pleural effusion in a child with ascites:

- Congenital pores are present on the right side of the diaphragm. Negative pressure is more on the right side. Hence, right-sided effusion is common in children with cirrhosis.
- Fluid in peritoneal cavity migrates across the diaphragm through the lymphatics.
- Ascitic fluid pressure leads to an increase in the intra-abdominal pressure. This results in the formation of blebs in the dome of the diaphragm which is ruptured.

CLASSIFICATION

Pleural effusion may be unilateral or bilateral. It can be classified as follows:

I. Based on the site of pleural fluid accumulation:
   1. Apical effusion
   2. Interlobar effusion
   3. Subpulmonic effusion
   4. Mediastinal effusion

II. Based on the mechanism of pleural fluid formation and type of fluid:
   1. Exudative
   2. Transudative

III. Based on the type of fluid in pleural space
   1. Pyogenic effusion (pus)
   2. Chylous effusion (lymph)
   3. Haemothorax (blood)
   4. Pseudochylous effusion
   5. Hydrothorax (serous fluid)

Exudative Effusion

It is due to an alteration in the local factors involved in the formation of pleural fluid. There may be an alteration in the pleural membrane permeability, increase in capillary wall permeability, vascular disruption or obstruction of lymphatic drainage of pleural space. There is an increase in the pleural fluid protein due to increased capillary permeability to proteins in the pleural space, as in inflammation, infection or invasion by malignant cells. The causes of exudative effusion are as follows:

1. Infective causes (pneumonia, lung abscess, bronchiectasis, pancreatitis and tuberculosis)
   - Bacterial—pneumonia, tuberculosis
   - Viral
   - Protozoal
   - Fungal
2. Collagen vascular disorders
   - Systemic lupus erythematosus (SLE)
   - Rheumatoid arthritis
   - Polyarteritis
3. Neoplastic—metastatic involvement of pleura occurs due to secondaries from adenocarcinoma of lungs, breast cancer, lymphoma and leukaemia. Leukaemia and lymphoma are common in children. Ovarian carcinoma, stomach cancer and sarcomas are also associated with pleural effusion
4. Uraemia
5. Drugs—Bromocriptine, amiodarone, nitrofurantoin, dantrolene, INH, PAS
6. Postradiation
7. Traumatic
8. Lung infarcts

Transudative Effusion

It is due to an alteration in the systemic factors that are involved in the formation of pleural fluid. This includes increased systemic or pulmonary hydrostatic pressure or decreased colloid osmotic pressure in the circulation. The permeability of pleural capillaries to the proteins is normal. Following are the causes of transudative effusion:

1. Renal cause—nephrotic syndrome
2. Cardiac cause—congestive cardiac failure
3. Hepatic cause—hepatic failure
4. Nutritional cause—protein energy malnutrition

5. Hypothyroidism

Differences between transudates and exudates are highlighted in Table 9.22.

TABLE 9.22 Differences between Transudate and Exudates

Features	Transudates	Exudates
Pathogenesis	Increased hydrostatic or decreased oncotic pressure	Inflammation or infiltration of pleura
Causes	Congestive cardiac failure, nephrotic syndrome, cirrhosis liver, hypoproteinemia	Parapneumonic effusion, empyema, tuberculosis
Appearance	Clear/straw-coloured	Cloudy, purulent, opalescent
Protein	Less than 3 g/100 mL	More than 3 g/100 mL
pH	>7.2 (7.3–7.5)	<7.2
Specific gravity	<1.018	>1.018
Glucose	>40 mg/dL	<40 mg/dL
LDH	Low, <200 IU/L	High, >200 IU/L
Clotting	Does not clot	Clots on standing
Frothing	Does not froth	Froths on shaking
Cells		
WBCs	<1000/mm^3	>1000/mm^3 >50% lymphocytes in tuberculous effusion >50% polymorphs in pyogenic effusion
Malignant cells	Absent	May be present
Gram staining/ acid fast staining	No organism	Organisms may be seen
Culture	No organism	Organisms may be cultured
Amylase in the pleural fluid	Negative	Present in pancreatitis
Pathology	Non-inflammatory	Inflammatory
Flow on tapping	Rapid flow	Slow flow

The differentiation between transudates and exudates is done by Light criteria and Roth's criteria.

Light criteria

At least one of the following criteria should be satisfied to identify exudates:

1. Pleural fluid to serum total protein ratio—more than 0.5
2. Pleural fluid to serum LDH ratio—more than 0.6
3. Pleural fluid LDH—more than two-third of serum LDH

None of these criteria should be satisfied in a transudative effusion.

Disadvantage of Light criteria: A number of cases of transudates are falsely classified as exudates by these criteria.

Roth's criteria

The differentiation between transudates and exudates is difficult by Light criteria in certain cases of high protein transudates (as in cardiac failure treated with diuretics). In such cases, the serum–pleural fluid albumin gradient is a better determinant. If serum–pleural fluid albumin gradient (g/dL) is more than 1.2 it is transudate, else exudates.

Pyogenic Effusion

Causative factors for pyogenic effusion:

- Lung abscess
- Septicaemia
- Chest wall injuries
- Rupture of oesophagus
- Rupture of subphrenic abscess
- Rupture of liver abscess

Chylous Effusion

Causative factors for chylous effusion:

- Trauma to thoracic duct
- Tumour (mediastinal lymphoma)
- Tuberculosis
- Lymphatic obstruction

Haemothorax

Causative factors for haemothorax:

- Chest wall injuries
- Bleeding disorders
- Neoplasms—leukaemia, lymphoma and mesothelioma
- Drugs—anticoagulants
- Pulmonary infarction

Pseudochylous or Chyliform Effusion

In this condition, as the name suggests, the pleural fluid is milky white and resembles chylous fluid. It is rich in cholesterol and does not contain any chylomicrons. It is usually postinflammatory but may be seen in long-standing cases of pleural effusion such as rheumatoid pleuritis, tuberculosis or paragonimiasis (lung fluke infection).

Hydrothorax

Non-inflammatory collection of fluid in the pleural cavity is known as hydrothorax. Fluid will be clear or straw-coloured. The most common cause is congestive heart failure followed by hepatic and renal failure. Transillumination test is positive in a case of hydrothorax. It is treated by treating the primary cause.

Bilateral Pleural Effusion

Pleural effusion is usually unilateral. But it can be bilateral in the following conditions:

- Congestive cardiac failure
- Hypoalbuminaemia
- Malignancy—lymphoma and leukaemias
- Systemic lupus erythematosus

Recurrent Pleural Effusion

It can occur in the following conditions:

- Pulmonary tuberculosis
- Congestive cardiac failure
- Collagen vascular disorders

Tuberculous Effusion

Characteristic features are as follows:

- Exudative pleural fluid
- Straw- or amber-coloured
- Formation of cobweb coagulum on standing
- Acid fast bacilli may be seen on acid fast staining
- Culture of pleural fluid may yield tuberculous bacilli
- The predominant cells in the pleural fluid are lymphocytes
- Pleural biopsy may be helpful in the diagnosis

Rheumatoid Effusion

Characteristic features are as follows:

- Pleural fluid is exudative in nature
- Predominant cells are lymphocytes
- Low glucose level in the pleural fluid
- Rheumatoid factor may be seen in the pleural fluid
- Antinuclear antibodies (ANA) may be present

Malignant Pleural Effusion

This type of effusion is characterised by recurrent effusion and blood-stained aspirate.

Cytological studies will reveal the presence of malignant cells. Following are the causes:

- Lymphoma
- Acute leukaemia

HISTORY TAKING

Presenting Complaints

These depend upon the amount of fluid and rate of accumulation.

- Chest pain
- Difficulty in breathing/shortness of breath
- Fever

Relevant Past History

- Tuberculosis
- Pleural tapping
- Skin rashes—SLE
- Trauma

EXAMINATION FINDINGS

Examination of Chest

Inspection Findings

- Absent or diminished movements on the affected side
- Hoover's sign—there is decreased chest movements on the affected side of the effusion
- Fullness of chest with bulging of intercostal space
- Tracheal shift to opposite side (Trail's sign)
- Mediastinal shift to opposite side
- Absent apical impulse or shifted to opposite side

Palpation Findings

- The findings of inspection are confirmed
- Vocal and tactile fremitus are absent

Percussion Findings

Stony dull note is present on percussion.

Traube's Space. This area overlies the fundus of stomach. Hence, it is normally tympanitic on percussion, but in cases of left-sided pleural effusion, it resonates a dull note.

Skodaic Resonance. The note may be resonant just above the level of effusion due to relaxation of the lungs at this level. This is called skodaic resonance.

Grocco's Triangle. It refers to a right-angled triangle of dullness in the posterior region of chest opposite to the side of effusion. It is due to mediastinal shift to the opposite side by a large pleural effusion.

Garland's Triangle. It is the small area of increase in relative resonance on the posterior chest wall on the side of a large pleural effusion.

Both Grocco's and Garland's triangles are seen in patients with unilateral moderate- to large-pleural effusion (Fig. 9.8).

Auscultation Findings

- Absence of breath sounds over the effusion
- Vocal resonance is absent
- Aegophony above the level of pleural effusion

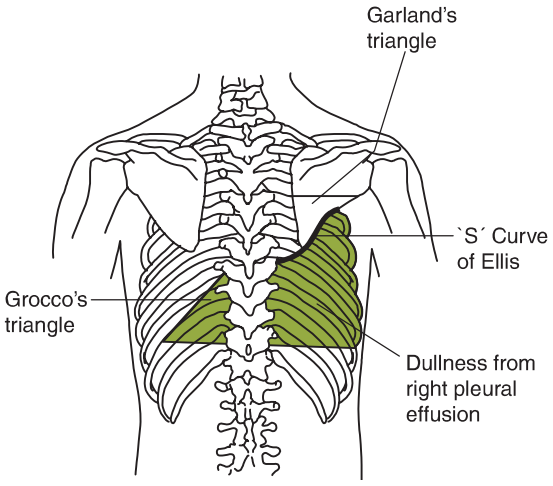


FIGURE 9.8 Percussion findings in pleural effusion.

(The patient is asked to say few words. The stethoscope is placed just above the level of the effusion. The words are heard like the bleating of a goat. This is due to relaxed lung above the level of pleural fluid.)

- Added sounds will be absent

INVESTIGATIONS

1. Total and differential leucocyte count
2. Radiological examination

(a) X-ray chest—Postero-anterior (PA) view is done in erect position. A total of 300 mL of pleural fluid is needed to diagnose pleural effusion clinically and radiologically in PA view. Even 50 mL of fluid can be demonstrated radiologically in lateral decubitus (Fig. 9.9). The findings present are:

- Obliteration of cardiophrenic and costophrenic angles
- Loculated effusions may be seen
- Subpulmonic effusion—Collection of fluid below the diaphragm will lead to elevation of diaphragm; the diagnosis is confirmed by X-ray in left lateral decubitus
- Lateral decubitus on the side of effusion will show a shift in the fluid level
- Tracheal and mediastinal shifts are seen in massive effusion

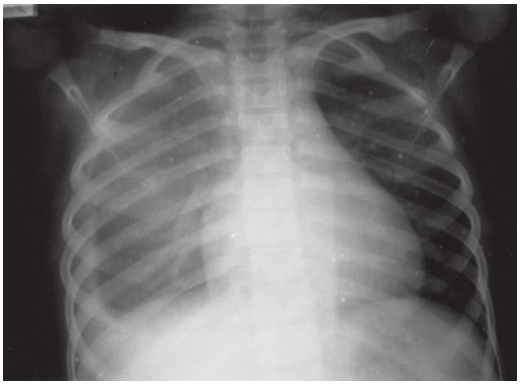


FIGURE 9.9 X-ray chest showing pleural effusion of the right side.

- Ellis curve—the level of fluid rises in the axilla as compared to the anterior and posterior levels. This is because the parietal and visceral pleura lie much closer at the lateral surface than on the other sides. Hence, due to capillary action, more fluid rises at the lateral part of the pleural surfaces. This gives rise to a raised radiographic shadow at the lateral parts.

(b) Ultrasonogram—it is useful in differentiating between loculated pleural effusion and tumour.
(c) CT scan—It may be helpful if the effusion is minimal or loculated.

3. Pleural fluid aspiration (thoracocentesis): Pleural fluid is collected in separate tubes for microbiological examination, cytology and biochemical analysis. Pleural tap is done to confirm and analyse the type of fluid in the pleural space. It helps to differentiate between exudates and transudates
4. Pleural biopsy: It can be done at a site with maximum dullness on percussion or at a point of maximum thickening of the pleura (as seen in the X-ray). Abram's pleural biopsy needle is used for pleural biopsy
5. Other investigations

(a) Mantoux test
(b) Resting gastric juice for tuberculous bacilli
(c) Bronchoscopy
(d) Biopsy or aspiration of an enlarged lymph node
(e) Serological tests—antinuclear antibodies, rheumatoid factors
(f) Pleural fluid complement is very low in rheumatoid and SLE related pleural effusions

Pleural Fluid Examination

Indications

1. Diagnostic—to differentiate between exudates and transudates
2. Therapeutic—pleural tapping is done as a therapeutic measure in the following conditions:
   - Massive collection or rapid collection of pleural fluid
   - Severe respiratory distress
   - Suspected empyema
   - Massive mediastinal shift

Precautions during Pleural Tap

- Pleural tap should be done under all aseptic precautions.
- Tapping should be done slowly.
- Needle should be inserted on the upper border of the lower rib. This is to prevent injury to neurovascular bundle present at the lower surface of the ribs.
- Ultrasound should be done in all cases to confirm the presence of pleural fluid.
- Tidal percussion is performed to confirm the upper border of liver.
- The tapping should not be done in cases of hydatid cyst, as an injury to the cyst may lead to leakage of fluid which can cause anaphylactic reactions.
- Large amount of fluid should not be taken out in a single sitting to prevent fluid and electrolyte imbalances.
- Tap should be done at the most dependent part, that is, the posteroinferior part of the lung.
- Site for loculated pleural effusion should be chosen under radiological guidance.
- Wide bore needle should be used to prevent a dry tap if there is thick pus.
- Injection atropine may be used to prevent pleural shock.

Gross Appearance

The appearance of the aspirated fluid should be examined. It may be

- straw-coloured,
- blood-stained,
- purulent,
- chylous.

Pleural Fluid Biochemistry

- pH
- Glucose
- Lactate dehydrogenase (LDH)
- Sodium, potassium and calcium concentrations
- Amylase
- Adenosine deaminase
- The ratio of protein in pleural fluid to serum
- Ratio of LDH values in pleural fluid and serum
- Pleural fluid can be tested for presence of tuberculous antibody, antigen and adenosine deaminase

Pleural Fluid Cytology

- WBC count
- Predominant cell type (neutrophil, lymphocytes, eosinophils, red blood cells)
- Lymphocytosis is present if 50% or more of the leucocytes are lymphocytes. Tuberculosis should be suspected in such cases
- Malignant cells

Pleural Fluid Microbiology

- Gram staining
- Acid fast staining for AFB
- Pleural fluid culture
- AFB culture
- PCR for tuberculosis

Features of Normal Pleural Fluid

- Clear ultra filtrate of plasma
- Glucose in pleural fluid is similar to that in plasma
- WBC count <1000 cells/mm^3
- Protein content <2% (1–2 g/100 mL)
- pH alkaline
- LDH levels <50% of plasma levels
- Sodium, potassium and calcium concentrations are similar to that in interstitial fluid

TREATMENT

Medical

1. Bed rest
2. Treat the cause
   - Pneumonia—appropriate antibiotics
   - Tuberculosis—antituberculous treatment along with corticosteroids is recommended for tuberculous patients with pleural effusion. Such patients are classified under category II based on classification of tuberculosis according to clinical types. A 2-month intensive phase therapy is followed by 4 months of continuation phase. The drug regime is 2HRZ/4HR (H—INH; R—rifampicin; Z—pyrazinamide). The three drugs are used for first 2 months followed by two drugs for the next 4 months. Prednisolone 1–2 mg/kg orally for 4–6 weeks promotes rapid absorption of the pleural fluid and prevents fibrosis
   - Congestive cardiac failure—treat with diuretics and other antifailure measures

Surgical

Open Drainage

Pleural fluid aspiration is done by using a wide bore needle. If the fluid is thick and cannot be drained by a needle, an intercostal drainage (under water seal) at the most dependant part should be done. Following are the intercostal drainage indications.

- Empyema
- Presence of causative organisms in the pleural fluid
- Pleural fluid glucose <50 mg/dL
- Pleural fluid pH <7.0.

Aspiration may be needed to relieve breathlessness. The complications of pleural aspiration are as follows:

- Pleural shock
- Introduction of infection
- Pneumothorax
- Pulmonary embolism
- Air embolism

- Acute pulmonary oedema
- Injury to neurovascular bundles
- Hydropneumothorax after pleural aspiration.

Pleurodesis

Effusions caused by malignancy usually reaccumulate; hence, it is advised to obliterate the pleural space by injecting substances (such as tetracycline), which will produce an inflammatory reaction and extensive pleural adhesions. The pleural fluid should be drained before the substances are injected into the pleural space.

Decortication

In children where the pus is organised or difficult to drain; the pleura may be removed.

The outer parietal pleura is stripped and resected. This enables reexpansion of the lung.

COMPLICATIONS

- Spread of infection to the adjacent area
- Collapse due to compression
- Empyema thoracis
- Thickened pleura
- Pulmonary oedema

PARAPNEUMONIC EFFUSION

It is a small effusion that usually occurs as a complication of bacterial pneumonia. Causes are as follows:

- Bacterial pneumonia
- Lung abscess
- Bronchiectasis

Pleural fluid examination findings are as follows:

- pH >7.2
- Glucose >40 mg/dL
- LDH <100 IU/L

Treatment

This condition is usually treated with appropriate antibiotics. Aspiration may be required if there is respiratory embarrassment due to massive collection of fluid. Thoracocentesis should be done if the thickness of fluid in a lateral decubitus X-ray is more than 10 mm.

Intercostal drainage with a test tube should be done if the fluid aspirated is grossly purulent or frank pus. The drainage can be removed if the draining fluid becomes serous or the amount collected per day is less than 50 mL.

TABLE 9.23 Differences between Pleural Effusion, Pyothorax and Thickened Pleura

Features	Pleural Effusion	Pyothorax	Thickened Pleura
Trachea	Pushed to opposite side	Pushed to opposite side	Normal
Fullness of chest wall	May or may not be present	Present with intercostal bulging	Flat
General condition	Non-toxic	Toxic	Non-toxic
Intercostal tenderness	Nil	Present	Nil
Source of septic foci	Usually absent	Present	Absent
Dullness	Stony dull	Stony dull	Dull

Prognosis

Most of the parapneumonic effusions resolve spontaneously without any treatment (Table 9.23).

EMPYEMA THORACIS

Empyema is a collection of pus in the naturally existing anatomical cavity. For example, collection of pus in the pleural cavity is known as empyema thoracis. Abscess is also due to collection of pus but it occurs in a newly formed cavity. Empyema thoracis is common in infants and young children. Predisposing conditions are as follows:

- Lung abscess
- Aspiration pneumonia
- Immunosuppression
- Trauma followed by superinfection

The common causative organisms are as follows:

- *Staphylococcus aureus*

- *Streptococcus pneumoniae*
- *Haemophilus influenzae* type B
- Pseudomonas, in sick children
- Anaerobic organisms

Infection may spread from any of the following sources:

- Infection in the lung (pneumonia)
- Blood (diverticulitis, cholangitis)
- Subdiaphragmatic abscess, ruptured esophagus, pericarditis, mediastinitis, osteomyelitis, etc.

PATHOGENESIS

Empyema is usually followed by parapneumonic effusion. This fluid is initially sterile but becomes infected later. This results in formation of pus. As the condition progresses, the fluid becomes thick. This is followed by thickening of pleura. There are three stages in the development of empyema (Table 9.24).

CLINICAL FEATURES

Symptoms

- Pleuritic pain in the early stages
- Fever
- Difficulty in breathing
- Cough

Signs

- Chest wall oedema on the affected side
- Empyema necessitans—pulsatile swelling over the chest
- Clubbing of fingers
- Dullness over the effusion
- Diminished or absent breath sounds on the affected side

INVESTIGATIONS

1. X-ray chest—It shows obliteration of costophrenic angle and varying degrees of opacification with or without mediastinal shift
2. Ultrasonogram
3. Diagnostic aspiration using a wide bore needle—Pleural tap is suggestive of purulent material full of pus cells with high protein and low sugar content. Bacteriological studies are done to identify the causative agent by gram staining and culture
4. Blood culture
5. CT scan shows presence of thick fluid in the pleural cavity

TREATMENT

The treatment should be started at the earliest. It consists of drainage of pus from the pleural cavity.

TABLE 9.24 Stages in the Evolution of Empyema

	Stages	Duration	Features
1	Exudative stage	24–72 hours	Increased pulmonary interstitial fluid due to outpouring of fluid with a low cellular content This occurs due to increased permeability of capillaries Pus accumulates Lungs are expansible Pleural fluid WBC, LDH levels are low, pH and glucose level is normal
2	Fibrinopurulent stage	3–10 days	Bacterial invasion of pleural space occurs Large quantities of pus accumulates with increased polymorphonuclear leucocytes Loculation of pus may be present Lungs become less expansible Pleural fluid pH and glucose levels are low Pleural fluid LDH level increases
3	Organising stage	10 days to few weeks	Proliferation of fibroblasts from both parietal and visceral pleura into the exudates produces an inelastic membrane known as pleural peel Scarring of pleural space with lung entrapment occurs Lungs become less expansible

Systemic antibiotics should be given to control the associated infections. The response to antibiotics is good in the early stages. In the later stages, surgical intervention is needed.

Stepwise Treatment

Aim	Mode
Control of infection	Appropriate antibiotics depending on the causative agent
Evacuation of pus	Needle aspiration Intercostal tube drainage Drainage under thoracoscopy
Restoration of normal respiratory function	Breathing exercises

Treatment includes the following neasures.

1. *Antibiotics* should be given based on the pus culture and sensitivity results (Table 9.25). Gram staining of the pus may identify the organism.
2. *Intercostal tube drainage*—usually the drainage tube is necessary for 1 week. The chest tube should be removed in the following conditions:
   - Pleural fluid becomes serous
   - The amount of fluid drained is <50 mL/day
3. *Instillation of fibrinolytic agents* such as urokinase, streptokinase is done into the pleural cavity if there is no improvement. This is helpful in children with organised emphysema or multiple loculations in the pleural space. A total of 250,000 units of streptokinase can be given in 30–60 mL of normal saline, intrapleurally through the chest tube. Urokinase can be given in a similar way in a dose of 10,000 units. The clamp should be closed for 1–2 hours after this. This can be repeated up to 14 days.
4. *Surgical treatment*—decortication is done by video-assisted thoracoscopic surgery or thoracotomy. Rib resection should be done to perform this.

TABLE 9.25 Choice of Antibiotics Based on the Causative Organisms

Organism	Antibiotics
Staphylococci	Cloxacillin: 100–200 mg/kg/day Vancomycin: 40 mg/kg/day Methicillin: 200–400 mg/kg/day
S. pneumoniae	Penicillin: G 1,00,000 units/kg/day
H. influenzae type B	Ampicillin: 100 mg/kg/day Chloramphenicol: 50 mg/kg/day Cefotaxime: 100 mg/kg/day Ceftriaxone: 75–100 mg/kg/day
Pseudomonas	Carbenicillin: 200–400 mg/kg/day Ticarcillin: 200–400 mg/kg/day

COMPLICATIONS

- Pyopneumothorax
- Rupture into the lung bronchopleural fistula, parenchymal–pleural fistula
- Rupture into peritoneal the cavity
- Rupture into the chest wall (empyema necessitans)

PROGNOSIS

Prognosis depends on the causative agent, stage at diagnosis and intervention. With adequate drainage and antibiotics, there is symptomatic improvement within 48–72 hours. Malignant effusion is associated with poor prognosis.

BRONCHIECTASIS

It is defined as abnormal and permanent dilatation of the bronchi, due to inflammatory destruction of bronchial and peribronchial tissue. There is persistent and irreversible destruction, distortion and dilatation of bronchioles of more than 2 mm in diameter.

AETIOLOGY

Congenital Causes

Arrest of bronchial development or defective development of the bronchial cartilaginous supports results in congenital bronchiectasis.

- Structural defects—familial deficiency of bronchial cartilage

- Kartagener's syndrome—bronchiectasis, sinusitis, situs inversus with ciliary dysfunction
- Young syndrome—azoospermia with normal spermatogenesis, sinusitis, rupture of subpleural emphysematous bullae
- Yellow nail syndrome—triad of lymphoedema of the extremities, deformed yellow nails, pleural effusion of unknown cause
- Cystic fibrosis—viscid mucous secretions
- Alpha-1-antitrypsin deficiency
- William–Campbell syndrome—bronchomalacia due to developmental defect of the bronchial cartilage
- Mounier–Kuhn syndrome—tracheobronchomegaly due to developmental defect in the elastic tissue
- Immunodeficiency syndromes—agammaglobulinaemia
- McLeod syndrome
- Middle lobe syndrome due to compression of the middle lobe bronchus
- Brown–Paterson syndrome
- Swyer–James syndrome

Acquired Causes

1. Necrotising inflammation
   (a) Bacterial
   (b) Viral-adenovirus
   (c) Fungal
   (d) Protozoal
   (e) Parasitic
2. Obstructive causes—bronchial obstruction
   (a) Luminal causes
      - Foreign body
   (b) On the wall of the tracheobronchial tree
      - Asthma
      - Tumours
   (c) Outside the wall
      - Lymph nodes
      - Rupture of subpleural emphysematous bullae
      - Left atrial enlargement
      - Aneurysms/abnormal vessels cause compression of the airways
3. Disorders of immunity
   (a) Allergy
   (b) Autoimmunity

PREDISPOSING FACTORS

1. Infections
   - Measles
   - Tuberculosis
   - Whooping cough
   - Endobronchial tuberculosis
   - Bronchiolitis
2. Aspiration
   - Anaesthesia
   - Dental extraction, oropharyngeal surgery
   - Aspiration due to near drowning, convulsions
   - Congenital defects such as tracheoesophageal fistula
   - Gastroesophageal reflux

PATHOLOGY

The first destructive change is loss of ciliated epithelium which is followed by destruction of elastic tissue. Generally, bronchiectasis follows a segmental distribution, except in cystic fibrosis. The commonly affected areas are right-middle segments, the basal segments of the lower lobes and the lingular segment of the left-upper lobe. The right-lower lobe is commonly involved in aspiration of the foreign body. The right-middle lobe is affected by hilar lymphadenopathy (Table 9.26).

TABLE 9.26 Anatomical Considerations Predisposing to Affliction of Particular Segments

Segments	Predisposing Factors
Basal segments of the left-lower lobes	Left main bronchus is small when compared to the right and crosses the mediastinum and aorta.
Right-middle lobe	Right bronchus arises at an acute angle and then bends forwards. Hilar nodes enlarge behind the right bronchus and cause obstruction.
Lingular segment of the left-upper lobe	More dependent in all positions such as erect, semirecumbent and lying down.
Right-lower lobe	Right main bronchus is larger and foreign body obstruction is common.

TYPES

1. True bronchiectasis
   (a) Saccular or cystic
   (b) Cylindrical
   (c) Varicose (intermediate)
   (d) Mixed
2. Pseudobronchiectasis (or reversible bronchiectasis)—it is a reversible condition unlike true bronchiectasis, which is irreversible. It is due to bronchial dilatation without destruction. It usually follows whooping cough and occurs in tracheobronchitis. Cylindrically dilated bronchi are seen in bronchography. Bronchography repeated after few months shows normal findings
3. Others
   (a) Bronchiectasis sicca (dry bronchiectasis)—in this condition, there is no production of sputum. Persistent cough with haemoptysis is present. It usually affects the upper lobes and is commonly seen in tuberculosis
   (b) Middle lobe bronchiectasis (Brock's syndrome)—it occurs in cases of pulmonary tuberculosis, where the right-middle lobe is commonly involved. It is compressed by the enlarged tuberculous lymph nodes. The right-middle lobe is commonly involved because
      - It is surrounded by lymph nodes
      - It originates in a narrow slit like lumen
      - It runs a long course
      - It is separated from the upper and lower lobes by fissures
      - It lacks collateral ventilation

CLINICAL FEATURES

The disease has an intermittently improving and relapsing course.

Symptoms

- Persistent cough—change in position or physical activity initiates bout of coughing
- Haemoptysis
- Copious, purulent, foul smelling sputum production
- Recurrent respiratory tract infections
- Dyspnoea
- Irritability
- Fever due to infections
- Loss of appetite
- Loss of weight

Signs

- Growth failure—poor weight gain
- Clubbing of fingers (not seen in congenital bronchiectasis and cystic lung disease)
- Halitosis
- Signs of cystic fibrosis (nasal polyp, features of sinusitis may be present)
- Signs of respiratory distress (intercostal recession, subcostal recession, etc.)
- Diminished breath sounds
- Rhonchi
- Coarse leathery rales/crepts
- Cardiac sounds are heard on the right side in dextrocardia associated with Kartagener's syndrome

INVESTIGATIONS

1. Complete blood count with peripheral smear
2. Radiological examination
   (a) X-ray chest
      - Railroad track appearance—marked linear streaking and loss of volume (crowding) over the area of bronchiectasis. This is due to dilated bronchioles and hyper inflated lungs
      - Honeycomb appearance may be seen due to dilatation of bronchus (Fig. 9.10)
      - Presence of cystic spaces (may contain fluid levels) more than 2 mm
      - Compensatory over inflation of other segments
      - Gloved finger appearance
      - Radio-opaque foreign body can be seen
   (b) X-ray sinuses may show evidence of sinusitis
   (c) CT scan—after inhalation of xenon gas, the scan is more sensitive. It shows four



FIGURE 9.10 X-ray showing bronchiectasis of left lung.

signs:

- Air fluid level in the distended bronchi
- Linear airway
- Distorted bronchi in the periphery of the lung
- Bronchial wall thickened by peribronchial fibrosis

(d) Bronchography
(e) Fluoroscopy is helpful if the foreign body is radio-opaque
(f) Ventilation perfusion scans using xenon gas
(g) MRI

3. Bronchoscopy—flexible fibroptic bronchoscopy is done for diagnosis and removal of the foreign body
4. Investigations for tuberculosis
   (a) Mantoux test
   (b) X-ray chest shows hilar lymphadenopathy
   (c) Sputum examination for acid fast bacillus
5. Sputum culture identifies the infecting organisms and their sensitivity to antibiotics
6. Assessment of ciliary function
   (a) It is done by placing a small piece of saccharine in the anterior part of nasal cavity and calculating the time it takes to reach the pharynx. The patient will feel the taste as the saccharine reaches the pharynx
   (b) Nasal mucosal biopsy to study the ciliary function
7. Sputum examination—colour, nature, quantity, gram staining and culture, staining for AFB, culture for TB bacilli, sputum for fungus
8. Sweat chloride estimation will be increased in cystic fibrosis
9. Immunoglobulin assay decreases in patients with immunodeficiency
10. Pulmonary function tests
11. Functional test for neutrophils
    (a) Nitroblue tetrazolium dye test
    (b) Chemotactic assay of neutrophils

TREATMENT

Medical

1. Antibiotics for 2–3 weeks
2. Treat the underlying causes
   - Eliminate all foci of infection
   - Remove foreign body
   - Antituberculous drugs—if pulmonary tuberculosis is present
3. Physiotherapy
   - Postural drainage—child is positioned in such a way so that the gravity helps in draining the mucus from the most congested area of the lung. For instance, if the left lung is involved, the child should be nursed in right lateral position to facilitate dependent drainage
   - Chest percussion—it is done by using a cupped hand, silicone percussion cup or a vibrating percussion machine. It is contraindicated when haemoptysis is present
4. Supportive treatment
   - Nutrition
   - Bronchodilators, aerosol therapy and mucolytics help in bringing out the sputum
   - Immunoglobulins in children with hypogammaglobulinaemia

Surgical

1. Lobectomy—removal of the lobe is done if the lesions are localised and the remaining lung is normal, in addition to one of the following:

- The condition is not responding to treatment
- Associated with a foreign body, which can not be removed by bronchoscope
- Localised anatomical defects
- Life-threatening haemorrhage
- Anatomical obstruction of the bronchi due to suppurative lesions

2. Lung transplantation is considered if the involvement is bilateral, extensive and not responding to medical therapy

COMPLICATIONS

- Haemoptysis (massive)
- Pneumothorax
- Pyothorax
- Lung abscess
- Metastatic abscess to the brain through vertebral plexus of veins
- Amyloidosis (rare)
- Cor pulmonale
- Pyaemia and septicaemia
- Cavity formation—small cysts fuse to form cavity
- Pleurisy
- Recurrent exacerbation leading to pneumonia and atelectasis
- Pulmonary osteoarthropathy

FOLLOW-UP

- Postural drainage and breathing exercises such as blowing a balloon and whistling are advised.
- In proven cases of bronchiectasis, influenza vaccine is given every year.
- X-ray is done once in 3 months to rule out superadded infections.
- Electrocardiogram is done to find right ventricular hypertrophy, which is seen in cor pulmonale.
- Sputum culture should be done frequently.

PROGNOSIS

Prognosis is good in the following cases:

- Young age
- Unilateral bronchiectasis
- Lower lobe lesions
- Good pulmonary function tests
- Treatable predisposing causes

PREVENTION

The following measures are helpful in preventing bronchiectasis:

- Early treatment of respiratory infections
- Immediate removal of foreign bodies
- Vaccination against measles, pertussis
- Treatment of predisposing factors such as GERD (gastroesophageal reflux disease), vascular ring compressing the respiratory passages.

EMPHYSEMA

Emphysema is a pathological condition of the lungs, which is characterised by abnormal increase in size of air spaces distal to terminal bronchioles either due to dilatation of the alveoli or from destruction of their walls, causing a decrease in lung function, and often, breathlessness.

PATHOPHYSIOLOGY

Pulmonary emphysema is a progressive chronic condition of the lungs in which there is destruction of the lung tissues which are necessary to support the physical shape and the function of the lungs. There is inflation of the bronchioles, alveolar ducts and alveoli with air. There is loss or weakening of elastic tissue which results in distended lungs which do not collapse during expiration.

Pulmonary emphysema may be associated with overdistension which may be followed by irreversible rupture of alveoli. The alveoli or air sacs may be destroyed, narrowed, collapsed, stretched or overinflated.

The air flow is affected which results in entrapment of air in the alveoli. This causes expansion of chest and shortness of breath.

Emphysema should be differentiated from reversible overinflation which occurs when there is distension of alveoli without any damage.

CLASSIFICATION

I. Classification according to aetiology
   1. Primary due to defects in the alveoli
   2. Secondary due to infections

II. Classification according to location (Table 9.27, see also Fig. 9.11):
   1. Centriacinar
   2. Paraseptal
   3. Panacinar
   4. Irregular

III. Classification according to the part of lung affected (Table 9.28):
   1. Alveolar emphysema
   2. Interstitial emphysema

Alveolar Emphysema

Alveolar emphysema may be generalised or localised (Table 9.29).

1. *Large lunged emphysema* or *hypertrophic emphysema.*

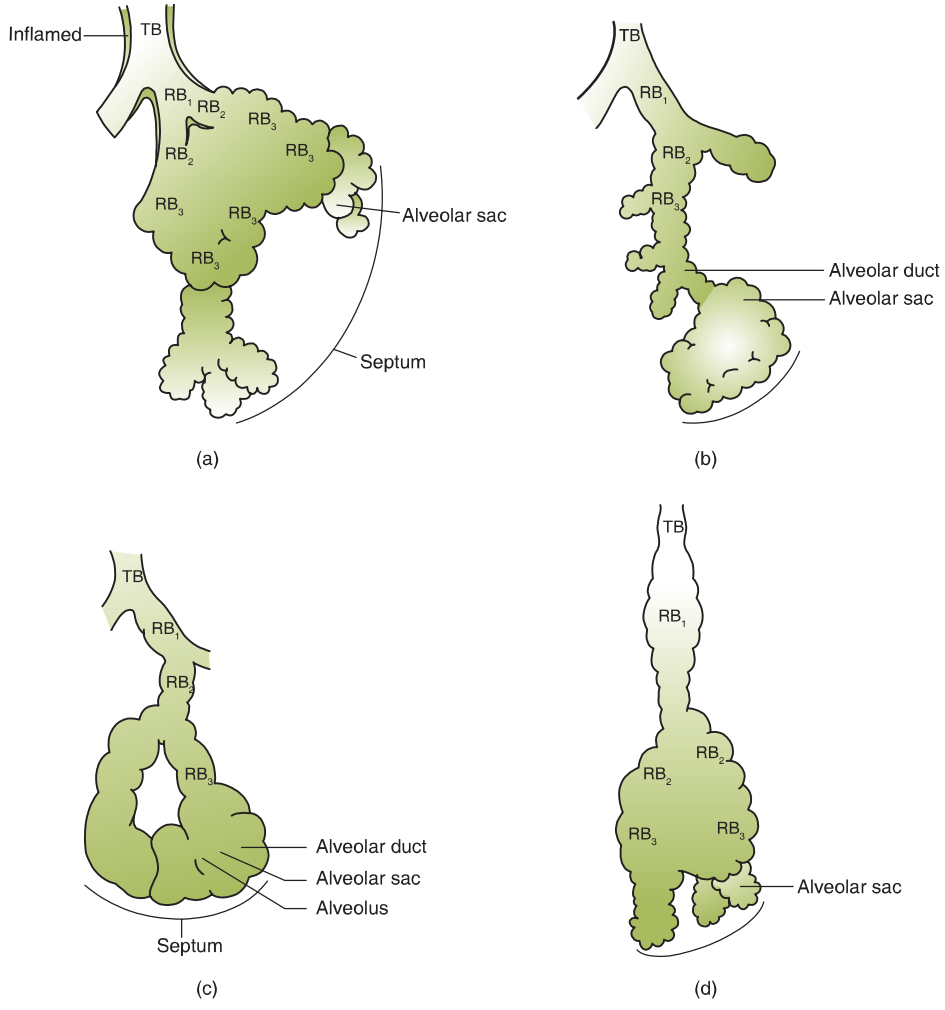


FIGURE 9.11 Types of emphysema. (a) Irregular. (b) Paraseptal. (c) Centriacinar. (d) Panacinar. TB—terminal bronchioles; RB—respiratory bronchides.

TABLE 9.27 Classification of Emphysema Based on Location

Features	Classification		
	Centriacinar /Centrilobular	Panacinar/Panlobular	Paraseptal/Distal Acinar
Pathology	The proximal part and the central part of the acinus will be affected. The distal acinus or alveoli will not be affected	Entire acinus from the respiratory bronchiole to the alveoli is affected	The distal acinus or alveoli will be affected. The proximal part and the central part of the acinus will be normal
Common sites	Upper lungs	Common on the lower lobe basal segments and anterior margins of lungs	Upper half of the lung adjacent to pleura
Etiological factors	Smoking	Alpha-1-antitrypsin deficiency Postobstructive	Pulmonary diseases/infections

TABLE 9.28 Types of Emphysema According to the Part of Lung Affected

Type	Pathophysiology
Alveolar emphysema	Emphysema occurs due to dilatation of the alveoli or from destruction of their walls
Interstitial emphysema	Rupture of the alveoli with extensive emphysema may be caused by vigorous resuscitative methods. The air from the lungs escapes along the perivascular spaces. Dilatation of air vesicles or rupture of the vesicles will result in escape of air into the connective tissue

TABLE 9.29 Alveolar Emphysema—Types

Type	Causes	Clinical Features
Generalised	Asthma Bronchiolitis Cystic fibrosis	Exertional dyspnoea Lungs overdistended
Localised	Foreign body obstruction Endobronchial tuberculosis Tracheobronchial lymphnode enlargement Intra bronchial tumours	Mediastinal shift to opposite side

2. *Small lunged emphysema* or *atrophic emphysema* is seen in elderly when the alveolar walls and septa undergo complete atrophy. The coalition of air sacs will result in formation of large air sacs. This is also known as senile emphysema.
3. *Compensatory emphysema* occurs when the total lung volume on one side is decreased due to any disease such as tuberculosis or lobar pneumonia, foreign body obstruction or surgical removal of part of the lung.

Other Types of Emphysema

Various terminologies used to describe some common types of emphysema are as follows:

- Overdistension emphysema occurs in bronchial asthma and partial obstruction by foreign body.
- Obstructive emphysema may be due to foreign body obstruction. Obstructive emphysema is associated with partial bronchial obstruction which will interfere with exhalation. The obstruction will cause partial air entry into the lungs and impaired expulsion.
- Unilobar emphysema/lobar emphysema involves less than all lobes of the lung hyperresonance over the affected lobe, mediastinal displacement. Lobectomy is the treatment of choice.
- Unilateral emphysema affects one lung.
- Atrophic emphysema—senile emphysema. Overdistension and stretching of lung tissues due to atrophic changes.
- Bullous emphysema—single or multiple large cystic alveolar dilatations of lung tissue.
- Congenital lobar emphysema–it is called infantile lobar emphysema. It occurs in infants when air enters the lungs but cannot leave easily. It most frequently affects the left upper lobe followed by the right middle lobe.
- Hypoplastic emphysema is due to developmental abnormality resulting in a reduced number of alveoli which are abnormally large.
- Interlobular emphysema is due to accumulation of air in the septa between lobules of the lungs.
- Pulmonary interstitial emphysema is seen in premature infants in which air leaks from the lung alveoli into the interstitial spaces.

PREDISPOSING AND PRECIPITATING FACTORS

- Violent straining due to cough
- Bronchitis
- Whooping cough
- Asthma
- Smoking
- Exposure to air pollutants, fumes, dusts, etc.
- Children with α-1 antitrypsin deficiency are prone to develop emphysema

HISTORY TAKING

Age

- Cystic fibrosis is usually seen in new born and early childhood.
- Foreign body aspiration can occur at any age, but is more common in toddlers.

History of Present Illness

Enquire about the clinical course of the disease.

1. Onset—H/o foreign body aspiration
2. Symptomatic
   - Fever
   - Difficulty in breathing
   - Haemoptysis

Past History

1. Repeated episodes of chest infections
2. History related to cystic fibrosis
   - Respiratory infections
   - Bulky, foul smelling stools
   - Failure to thrive
   - Malabsorption (pancreatic insufficiency in cystic fibrosis)

Personal history

- H/o smoking is important in adults.

History of Contact

- H/o contact with a known case of tuberculosis.

Family History

- Cystic fibrosis
- Alpha-1 antitrypsin deficiency

Socioeconomic History

- H/o exposure to toxic substances.

EXAMINATION FINDINGS

General Examination

- Cyanosis
- Exertional dyspnoea
- Double expiratory effort (broken wind)
- Jugular venous pressure increased

Chest Examination

1. Inspection
   - Chest wall movements decrease
   - Use of accessory muscles of respiration—contraction of sternomastoid and scalene muscles on inspiration in drawing of costal margin
   - Tracheal descent with inspiration—as the chest cavity is distended further expansion of lungs will cause the movement of trachea down into the thorax
   - Tracheal length in the neck decreases
   - Barrel-shaped chest—anteroposterior diameter increases
   - The sternum, scapula and clavicles appear prominent
2. Palpation—anteroposterior diameter of the chest increases
3. Percussion—hyperresonant percussion is noted
4. Auscultation
   - Breath sounds—diminished vesicular sounds with prolonged expiration
   - Expiratory rhonchi/wheeze
   - Fine crepts
   - Vocal resonance reduced or normal

CLINICAL FEATURES

Common symptoms are as follows:

- Cough
- Difficulty in breathing/shortness of breath

Other features are as follows:

- Fatigue
- Central cyanosis
- Purse lipped breathing
- Wheezing
- Secondary polycythaemia due to hypoxia
- Asterixis due to retention of carbon dioxide

DIAGNOSIS

The specific diagnosis is made only by pathological studies. However, the condition can be diagnosed by the following:

1. History
2. Physical examination
3. Radiological changes
4. Pulmonary function tests

INVESTIGATIONS

1. Radiological features
   (a) X-ray chest
      - Hyperinflation
      - Diaphragm pushed down
      - Generalised obstructive overinflation

   (b) Fluoroscopy
      - Hyperventilation of the lungs
      - Diaphragm pushed down with decreased movements
2. Pulmonary function tests—increased residual lung volume
3. Oxygen saturation studies—blood analysis to monitor the levels of carbon dioxide and oxygen in the blood. It shows low PaO_2
4. Sputum examination for presence of any infective agent

COMPLICATIONS

R	Respiratory failure
E	Expiratory dyspnoea
S	Subpleural bullae may rupture to produce spontaneous pneumothorax
P	Pulmonary hypertension
I	Interstitial emphysema
R	Right ventricular failure
A	Air leak into the mediastinum (pneumomediastinum)

TREATMENT

1. Treat the associated infections
2. Physiotherapy
3. Supportive therapy
   - Oxygen supplementation—hospital/domiciliary oxygen
   - Bronchodilators
   - Anticholinergics
   - Oral or inhaled steroids
   - Fluid replenishment
4. Surgical treatment
   - Lung volume reduction surgery—reduction of lung by removing the damaged area of the lung by surgical procedures such as lobectomy
   - Lung transplantation in more severe cases
5. Pulmonary rehabilitation—teach the patient about the breathing exercises, avoidance of air pollutants, and improving the quality of life

PREVENTION

- Avoid precipitating agents such as exposure to pollutants, smoking and so on
- Treat infections with appropriate antibiotics
- Vaccination with pneumococcal and influenza vaccines as per recommendations

PNEUMOTHORAX

Pneumothorax is a condition where there is collection of air in the pleural cavity.

CAUSES

1. Traumatic—this includes penetrating/non-penetrating wounds
2. Spontaneous
   - Rupture of subpleural emphysematous bullae
   - Rupture of congenital cyst
   - Rupture of tuberculous cyst in the lung
   - Rupture of a tension cyst in the lung
3. Iatrogenic
   - Following vigorous bag and mask ventilation, especially in newborn babies during resuscitation
   - Following intercostal tube insertion
   - Thoracocentesis
   - Following cardiothoracic surgery
4. Miscellaneous—this includes foreign body obstruction

TYPES

1. *Closed pneumothorax:* This is usually due to rupture of an emphysematous bulla. The opening in the pleura closes and the communication between the lung and the pleural space is closed. The symptoms are not severe. The intrapleural pressure is lower than that of the atmospheric pressure. The opening of the lung is small and it heals spontaneously.
2. *Open pneumothorax:* Opening remains patent. Pressure in pleural cavity is equal to that of atmospheric pressure.
3. *Tension pneumothorax:* It is of valvular type. Air enters into pleural space during inspiration but cannot escape. This leads to entrapment of large volume of air in the pleural space. Dyspnoea is very severe. There is progressive mediastinal shift. Central cyanosis may be present. This is a medical emergency.

HISTORY TAKING

History of Present Illness

Enquire about the clinical course of the disease.

1. Acute onset
2. Symptomatic
   - Dyspnoea at rest
   - Chest pain is stabbing in nature. It is aggravated by laughing, crying, inspiration, chest movements and coughing
3. Short duration

History of Past Illness

- Cough—usually precipitates pneumothorax
- Tuberculosis
- Injury
- Haemoptysis
- Similar illness in the past

EXAMINATION FINDINGS

General examination is done as for other respiratory diseases. Tachypnoea is usually present in a case of pneumothorax.

Chest Examination

1. Inspection
   - Mediastinal shift to opposite side
   - Fullness of intercostal spaces
   - Chest movements are diminished on the affected side
2. Palpation
   - Trachea is shifted to the opposite side
   - Apical impulse is shifted to the opposite side
   - Chest movements are diminished on the affected side
   - Chest expansion is decreased
   - Vocal fremitus and vocal resonance is diminished or absent
   - No local tenderness
3. Percussion
   - Hyper-resonance note on the affected side
   - Liver dullness is shifted down

- Normal percussion note is present on the unaffected side

4. Auscultation
   - Breath sounds are diminished or absent
   - Vocal resonance is diminished or absent on the affected side
   - Absence of added sounds
   - Coin test positive—a metallic coin is placed on the chest wall anteriorly or posteriorly, over the affected part. This coin is tapped by another coin and auscultated by placing the diaphragm of the stethoscope on the corresponding back/front side. In patients with pneumothorax, a high-pitched, tympanitic metallic sound will be heard. This should always be compared with the normal side

INVESTIGATIONS

1. To confirm the diagnosis—X-ray chest is done in erect posture. An expiratory film is helpful. Following are the radiological features.
   (a) Increased radiolucency on the affected side, with absent lung markings
   (b) Collapsed lung on the affected side
   (c) Shift of mediastinum to the opposite side
2. To find out the aetiology
   (a) Total blood count
   (b) Differential blood count—increased lymphocytes in tuberculosis
   (c) Erythrocyte sedimentation rate (ESR)—may be raised in infections
   (d) In tuberculosis, the following investigations are suggestive:
      - Mantoux test is positive in tuberculosis.
      - BCG test—accelerated BCG reaction is seen in malnourished children, where the mantoux test may be false-negative
      - Sputum examination is done for acid fast bacilli for three consecutive days. Young children usually swallow the sputum. So, examination of the gastric contents (aspiration of the resting gastric juice) for acid fast bacilli early in the morning will be useful in such children
      - Radiological evidence of tuberculosis
3. To asses the severity—lung function tests help in assessing the severity. They also help in monitoring the improvement. The following values will be decreased in pneumothorax:
   (a) Tidal volume
   (b) Forced expiratory volume in the first second (FEV_1)
   (c) Forced vital capacity (FVC)
   (d) Peak expiratory flow rate (PEFR)

MANAGEMENT

1. Small pneumothorax—The air gets absorbed spontaneously. Hence, no treatment is usually required. Rarely surgical intervention may be needed if the air is not absorbed, causing respiratory distress and cyanosis.
2. Tension pneumothorax—This is a surgical emergency and should be treated immediately. The patient should be placed in a propped-up position. A self-retaining catheter is inserted into the pleural cavity in the second intercostal space along the midclavicular line, with the patient in the sitting position. The tube should be connected to the water seal drainage system. Oxygen inhalation should be given. The tube is removed if there are no air bubbles for 24 hours and the patient is relieved of symptoms. This may take 3–4 days.
3. Recurrent spontaneous pneumothorax—Chemical pleurodesis is done to obliterate the pleural space to prevent recurrence of pneumothorax. Some irritants are injected into the pleural space, which cause inflammation and adhesion of the pleural surfaces, thereby obliterating the pleural space. Talcum, minocycline, 50% glucose solution can be used for this purpose.
4. Antibiotics should be used to treat the infection. Also, it can be used as a prophylactic measure to prevent infections in children with predisposing conditions.
5. Antituberculous treatment should be given if the patient is suspected to have tuberculosis.
6. Surgical treatment
   - Decortication
   - Closure of bronchopleural fistula
   - Excision of the bulla
   - Lobectomy
   - Thoracoplasty

COMPLICATIONS

- Hydropneumothorax
- Pyopneumothorax
- Empyema thoracis
- Thickened pleura
- Atelectasis of lung
- Surgical emphysema and pneumomediastinum
- Bronchopleural fistula

PROGNOSIS

Prognosis of the pneumothorax depends on the following factors:

- Type of the pneumothorax—spontaneous pneumothorax has a good prognosis while tense pneumothorax has a bad prognosis.
- Cause—rupture of subpleural emphysematous bullae has a good prognosis.
- Time of intervention—early intervention has a good prognosis.
- Complications—in the absence of infections and complications such as hydropneumothorax, bronchopleural fistula, early intervention will have a very good prognosis

HYDROPNEUMOTHORAX

In this condition both air and fluid are present in the pleural cavity, unlike pneumothorax where only air is present in the pleural cavity, or pleural effusion, where only fluid is present.

CLINICAL FEATURES

In addition to the features of effusion and pneumothorax, the following features (4S) are also present:

- Straight line dullness—the level of dullness due to fluid in the pleural cavity is straight
- Shifting dullness
- Succussion splash
- Sound of coin

Typical physical signs in common respiratory disorders

Pathological process	Movement of chest wall	Mediastinal displacement	Percussion note	Breath sounds	Vocal resonance	Added sounds
Consolidation	Decreased on the same side	Absent	Impaired	High-pitched bronchial	Increased	Crepitations early: coarse Later: none
Collapse due to obstruction of major bronchus	Decreased on the same side	Same side	Dull	Decreased or absent	Decreased	Absent
Collapse due to distal bronchial obstruction	Decreased	Same side	Dull	High-pitched bronchial	Increased	Absent
Pleural effusion	Decreased	Opposite side	Stony dull	Decreased or absent	Decreased or absent	Aegophony above the level of effusion
Pneumothorax	Decreased or absent	Opposite side	Hyperresonance	Decreased or absent	Decreased or absent	Absent
Bronchiectasis	Slightly reduced	Absent	Impaired	Low pitched	Increased	Coarse crepitations

CHAPTER 10

Disorders of Gastrointestinal System

HISTORY TAKING

Abdominal symptoms may be a manifestation of extra-abdominal disorders. Some extra-abdominal manifestations may be seen in abdominal diseases. For instance, diabetic ketoacidosis can present with abdominal pain; hypoproteinaemia can present with ascites; increased intracranial tension, as in meningitis, may present with vomiting. Hence, a careful detailed history should be elicited to diagnose abdominal disorders.

Name

Name can give a clue about the country to which the child belongs. Many disorders such as malaria and tuberculosis are common in endemic areas.

Age

Many abdominal disorders are age-specific. The age of patients can give the examiner some clues regarding the condition they could be suffering from. Some examples of age-specific disorders that present with abdominal symptoms are listed as follows:

- Glycogen storage disorders present with hepatosplenomegaly. The affected children present at an early age with symptoms such as early morning hypoglycaemia. Glucose-6-phosphatase dehydrogenase (G6PD) deficiency is seen in infants.
- Acute lymphatic leukaemia presents with hepatosplenomegaly and is common in the age group of 2–10 years.
- Hodgkin's lymphoma presents with hepatosplenomegaly and has a bimodal presentation. It is rare before 5 years of age and affects the age group of 15–34 years and then above 50 years of age.
- Hepatosplenomegaly due to thalassaemia usually presents after the age of 6 months.
- Cystic fibrosis may manifest in the newborn period with meconium ileus.
- Wilson's disease usually manifests after 5 years of age.

Gender

Certain disorders are more common in a particular gender. For example, Wilson's disease and Reye's syndrome are more common in boys. Idiopathic hypertrophic pyloric stenosis is also seen more commonly in boys. Ovarian cyst and haematocolpos are seen in females. Haemochromatosis is not common in females after puberty as there is blood loss during menstruation.

Race

Cystic fibrosis is more common in Whites.

Place

Certain diseases are endemic in particular parts of

the world. One should know the common diseases prevalent in their areas. For example, thalassaemia is common in Mediterranean areas (among Greeks and Italians), China, Malaysia and India.

Presenting Complaints

The examiner should record the presenting complaints in the informant's/patient's own words. The onset of symptoms should always be recorded in the chronological order of their appearance.

Example of presenting complaints in chronological order of appearance

- Vomiting—7 days
- Yellowish discolouration of the eyes—5 days
- Decreased urine output—3 days

History of Present Illness

The child should be enquired about the onset and progression of symptoms. Also, any factors which have precipitated or relieved the symptoms should be enquired. For example, pain due to gastritis is relieved by bland diet or antacids. Many systemic disorders can present with abdominal symptoms; therefore, history related to systemic disorders should also be enquired. For instance, diabetic ketoacidosis may present with acute abdominal pain.

Abdominal Symptoms

Abdominal symptoms depend on the site of pathology. The child presents with abdominal pain, loss of appetite, vomiting, dysphagia, flatulence, haematemesis and melaena when the upper alimentary tract is involved. When the lower alimentary tract is involved, the child may present with abdominal pain, diarrhoea, constipation and haematochezia. A few of the common abdominal symptoms are listed as follows:

- Vomiting—forceful expulsion of gastric contents through the mouth. It may be due to reflex irritation of the stomach or may have central origin.
- Nausea—unpleasant epigastric sensation with increased salivation.
- Retching—strong involuntary effort to vomit.
- Regurgitation—effortless return of gastric contents to mouth.
- Abdominal pain—colicky pain is seen in any condition that results in obstruction of intestines or any tubular structures; crampy pain is seen in Crohn's disease.
- Abdominal distension—seen in obstruction of gastrointestinal tract (GIT), paralytic ileus and hypokalaemia, which is commonly seen in diarrhoea.
- Constipation—difficult, infrequent passage of stools.
- Diarrhoea—increase in frequency, fluidity or weight of the stool. Weight of stool of a normal child is 5–10 g/kg/day. In diarrhoea, it is more than 10 g/kg/day.
- Encopresis—involuntary passage of stools at inappropriate places after 4 years of age.
- Haematemesis—vomiting of blood. It is seen commonly in rupture of oesophageal varices or superficial tear of oesophageal mucosa at gastro-oesophageal junction due to vomiting (Mallory–Weiss syndrome).
- Rectal bleeding—passage of blood in the stools. Haematochezia is the term used for passage of frank blood per rectum.
- Melaena—passage of black tarry stools due to bleeding in the GIT above the ligament of Treitz. This blood is converted into acid haematin by the hydrochloric acid from the stomach.
- Jaundice—yellowish discolouration of skin, mucous membrane and conjunctiva due to excessive accumulation of bile pigments in the blood. Jaundice occurs when the production of bilirubin exceeds the capacity of the liver to conjugate, or there is hepatic damage or obstruction to the flow of bile.
- Pruritis—seen in hepatic failure due to increase in bile salts.
- Dysphagia—difficulty in swallowing. There are three phases in swallowing: oral, pharyngeal and oesophageal. Disorders of the mouth, pharynx or oesophagus can result in dysphagia. It is also seen in structural or motility disorders of oesophagus.
- Heart burn—pain in the epigastrium and chest due to reflux of acidic contents of the stomach into the oesophagus.

Abdominal Pain. Abdominal pain is a commonly reported symptom in paediatric age group. The clinician should note the following aspects when enquiring about abdominal pain:

- Onset—the onset may be acute or insidious.
- Site—the clinician should note whether the child localises the pain to a particular site with a finger or over an area with a hand.
- Radiation—the clinician should enquire whether the pain is located at the same site or spreads to other parts of the body and should also ask if the spread is gradual or shooting in nature.
- Severity of the pain—the intensity of pain may vary from mild to severe. If the pain is mild, the child may only complain of pain. If the pain is severe, the child may present with incessant crying or restlessness, depending on the age.
- Timing and duration—the clinician should enquire about the time of onset of pain, its duration and whether it has improved or deteriorated with time. A nocturnal pain which occurs during sleep is usually associated with organic lesions such as gastro-oesophageal reflux.
- Character of pain—the clinician should ask if the pain is stabbing, burning, colicky, pricking or gnawing in nature.
- Aggravating and relieving factors—the clinician should enquire about the factors that cause or intensify the pain. Any factors which reduce the pain should also be enquired.

Vomiting. Vomiting is seen in many GI disorders such as intestinal obstruction, inflammatory bowel disease, gastroenteritis and disorders of liver. If the informant/patient reports vomiting, the clinician should enquire about the following:

- Time of onset of vomiting after the food intake—the timing can point out possible aetiological factors. For instance, in pyloric stenosis vomiting occurs immediately after ingestion of food.
- Number of episodes—vomiting after every feed may be psychogenic or may occur due to intestinal obstruction.
- Type of vomitus—the type of vomitus can help in diagnosing the condition. For instance, the bilious or non-bilious nature of vomitus can point out the site of obstruction (Table 10.1).
- Projectile/non-projectile—projectile vomiting is seen in idiopathic pyloric stenosis.
- Contents of the vomitus—the clinician should enquire whether the vomitus contains any undigested food particles (Table 10.2).
- Associated events—the clinician should ask about any associated events. They could point towards possible causes of vomiting (Table 10.3).

Diarrhoea. In case the patient has diarrhoea, the clinician should enquire about the following aspects:

TABLE 10.1 Site of Obstruction Derived from Type of Vomitus

Type of Vomitus	Site of Obstruction
Bilious	Distal to ampulla of Vater
Non-bilious	Proximal to ampulla of Vater

TABLE 10.2 Contents of the Vomitus

Contents	Conditions
Food particles undigested	Gastric outlet obstruction
Blood tinged	Gastritis or mucosal damage
Bile tinged	Intestinal obstruction distal to ampulla of Vater
Faeculent	Gastrocolic fistulas, distal intestinal obstruction

TABLE 10.3 Associated Events with Vomiting

Associated Events	Possible Causes
Jaundice	Hepatitis
Loose stools	Gastroenteritis, malabsorption, pancreatic insufficiency
Headache, convulsions or fever	CNS infections
Constipation	Intestinal obstruction
Vomiting after several hours of taking food	Gastric outlet obstruction Food poisoning
Pain in right iliac fossa	Acute appendicitis
Burning micturition	Urinary tract infection
Ball rolling movements in the abdomen	Intestinal obstruction
No nausea or anorexia	Psychogenic vomiting

TABLE 10.4 Nature of Stools and Possible Causes of Diarrhoea

Nature of Stools	Possible Causes of Diarrhoea
Watery stools	Secretory diarrhoea Rotavirus infection
Rice-water stools	Cholera
Foul-smelling stools	Fat malabsorption
Blood-stained stools	Dysentery due to *Shigella*, enteroinvasive *E. coli* Ulcerative colitis

- Onset—the clinician should enquire about the mode of onset (acute/insidious).
- Nature of stools—the nature of stools can also guide the clinician to the possible cause of diarrhoea (Table 10.4).
- Type of food taken recently—this can point out possible food poisoning/allergies. For instance, mushroom taken by a family may be associated with food poisoning. Aflatoxin-containing food is hepatotoxic.
- Time interval between food intake and onset of diarrhoea—this can point out possible causative factors. For example, the incubation period for staphylococcal food poisoning is 2–3 hours.

Constipation. In cases with constipation, the following points should be enquired:

- Onset from birth is seen in hypothyroidism.
- Acute onset without any preceding symptoms may be due to intestinal obstruction.
- Passage of flatus—if the patient is not passing stools as well as flatus, it is called obstipation.
- Frequency of stools—child may pass stools once in 2 days or more.
- Altered consistency of stools—stools become dry and hard.
- Difficulty in passing stools—child strains to pass stools.
- Pain during defecation—this should prompt the examiner to look for anal fissures.
- Associated symptoms if any—for instance, intolerance to cold occurs in hypothyroidism.

Abdominal Distension. Abdominal distension may be due to collection of fluid in the abdominal cavity (ascites). The following points should be enquired:

- Onset—sudden onset is seen in acute Budd–Chiari syndrome and acute right-sided heart failure. Insidious onset is seen in decompensated cirrhosis and tuberculosis abdomen.
- Duration.
- Progressive/static/regressive.
- Preceding events—anorexia, diarrhoea, constipation, etc. Postanorexial onset of abdominal distension may be due to infection of peritoneum. Peritonitis predisposes to paralytic ileus. Postdiarrhoeal onset may be due to paralytic ileus precipitated by hypokalaemia. Postconstipational onset may be due to intestinal obstruction.
- Associated with fever/pain in the abdomen.

Jaundice. Liver disorders are associated with increased bilirubin.

- Onset—sudden or insidious. Sudden onset is seen in obstructive jaundice. Insidious onset is seen in hepatitis.
- Duration—the duration of jaundice can lead the clinician to the possible underlying cause of jaundice. For example, chronic jaundice is a feature of cirrhosis and chronic hepatitis.
- Associated features—for example, clay-coloured stools are seen in obstructive jaundice.

Gastrointestinal Bleed. Character of bleed from GIT is helpful in identifying the site of the lesion in the gut. The acid in the stomach converts haemoglobin into acid haematin if the bleeding is above the duodenojejunal ligament (ligament of Treitz). This results in passage of black and tarry stools. Passage of frank blood in stools indicates that the lesion is near the rectum. Different terminologies used for GI bleed are as follows:

- Haematemesis—vomiting of fresh blood. Recurrent episodes are associated with oesophageal varices.
- Melaena—passage of black tarry stools. The stools are sticky and offensive. The minimum amount of GI bleed needed to cause melaena is 50–100 mL. Blood has to stay in the intestines for at least 6 hours to produce melaena.

- Haematochezia—passage of frank blood per rectum. This occurs when the bleeding is from the lower GIT (below the ligament of Treitz). Bleeding from haemorrhoids is a common cause.

Assessment of blood loss: The clinician should enquire about the following to assess the amount of blood loss (Table 10.5) and to decide if blood transfusion is necessary.

- Onset—acute onset is dangerous and may need immediate replacement. In chronic blood loss, the body maintains a normal haemostasis by mobilising fluid from other tissue compartments.
- Number of episodes—if the number of episodes is more, the blood loss may be more even if the quantity of blood loss is small. Recurrent episodes of haematemesis may be due to oesophageal varices. If there is frequent blood loss, the body will not have enough time to adapt. Hence, intervention should be done immediately.
- Quantity of blood in each episode—more than one fist of blood signifies a major bout. This is important as the child adapts to minimal blood loss by increase in cardiac output and mobilisation of fluid from extravascular to intravascular compartment. If the blood loss is massive, the body cannot adapt and may present with shock and hypotension.
- Precipitating factors—bleeding may be precipitated by specific drug intake.

TABLE 10.5 Clinical Features to Determine the Quantity of Blood Loss

Quantity of Blood Loss	Features
Mild bleeding	No significant fall in haemoglobin; does not require blood transfusion after the bleeding.
Moderate bleeding	Significant blood loss with tachycardia, hypotension and altered sensorium. This condition needs blood transfusion. There is no ongoing blood loss.
Severe/massive bleeding	This takes longer time to recover and requires multiple blood transfusions. The mortality is high. Any of the following features is present: • At least one fist of blood loss • Melaena >3 days • Significant fall in haemoglobin to about 8 g% in a previously normal child • Presents with shock, does not respond readily to volume replacement therapy • There is ongoing blood loss

Urinary Symptoms. The colour of urine gives a clue to the type of disorders causing jaundice. The urine is colourless (acholuric in obstructive jaundice). Haematuria is seen in urinary tract infections. History of altered bladder habits such as oliguria, anuria and polyuria should be noted.

Fluid Retention. The collection of fluid may begin in the abdomen or other parts of the body, giving a clue to the aetiology. The clinician should enquire about the mode of onset and progression of the fluid retention. The area of onset often points out the organ involved (Table 10.6).

Extra-Abdominal Features of GI Disorders

Many disorders of the GI system present with extra-abdominal features in addition to the common GI symptoms. Some of these are given in Table 10.7.

TABLE 10.6 Causes of Fluid Retention Based on Area of Onset

Area of Onset	Organs Involved
Face	Renal causes (hepatorenal syndrome)
Abdomen	Hepatic causes (hepatic cirrhosis)
Pedal oedema	Cardiac causes (cardiac cirrhosis)
Generalised oedema (anasarca)	Nutritional (kwashiorkor)

TABLE 10.7 Extra-Abdominal Manifestations of Gastrointestinal Diseases

Features	Diseases
Joint pain (arthritis) Pain in the eye (uveitis, episcleritis) Skin rashes (erythema nodosum)	Inflammatory bowel diseases such as Crohn's disease and ulcerative colitis
Night blindness (eyes—Bitot's spots)	Cholestasis, malabsorption syndrome
Altered sensorium, jaundice	Liver cell failure

The clinician should also enquire about any other associated features that may help in diagnosing the condition. The relevant associated features include the following:

- H/o skin changes (such as paddy field dermatosis and flaky paint dermatosis) may indicate malnutrition states such as kwashiorkor.
- H/o itching or purpura with jaundice indicates liver failure.
- H/o perianal excoriation is seen in acrodermatitis enteropathica.
- H/o upper abdominal discomfort in the presence of dyspnoea, palpitation or chest pain usually indicates congestive cardiac failure (CCF).
- H/o loss of appetite is seen in viral hepatitis and liver cell failure.
- H/o loss of weight is seen in malabsorptive disorders.
- H/o altered behaviour is associated with Wilson's disease (hepatolenticular degeneration).
- H/o altered sensorium and altered sleep rhythm are associated with hepatic encephalopathy.
- H/o early morning convulsions or dizziness may indicate hypoglycaemia due to glycogen storage disorders.
- H/o joint pain and swelling may be due to arthritis in inflammatory bowel disease.
- H/o rashes (Henoch–Schonlein purpura presents with rashes and abdominal pain).
- H/o passing worms in stools is a clear indication of worm infestation.
- H/o pica is commonly associated with iron deficiency anaemia and may result in worm infestation.
- H/o symptoms of fat-soluble vitamin deficiencies occur due to fat malabsorption in malabsorption and liver disorders (Table 10.8). Spontaneous or excessive GI bleeding may indicate a bleeding diathesis due to vitamin K deficiency.

TABLE 10.8 Features Associated with Deficiency of Fat-Soluble Vitamins

Fat-Soluble Vitamin	Manifestations in Deficiency
Vitamin A	Night blindness
Vitamin D	Rickets
Vitamin E	Haemolytic anaemia, neuropathy, myopathy
Vitamin K	Bleeding

History of Past Illness

Some conditions may present with recurrent symptoms. Past history gives information about the previous status of organs (such as liver) or the presence of chronic conditions. The following points are relevant to a patient with GI complaints and should be noted in past history:

1. Jaundice—this indicates the presence of chronic liver disease. The following points should be enquired:
   - Number of episodes
   - Details of each episode—onset, progression, intensity
   - Associated features—pruritis (due to the presence of bile salts), high-coloured urine (obstructive jaundice), staining of stools. In extrahepatic biliary atresia (EHBA), the stools are not bile stained. In neonatal hepatitis, the stools may be bile stained intermittently
   - Recovery—rapid/slow
2. GI bleeds—recurrent bleed may indicate the presence of portal hypertension of long duration.
3. Passing worms in stools may indicate a relapse of worm infestation in the current illness.
4. Tuberculosis—ascites in a patient with past history of tuberculosis is likely to be due to tuberculous peritonitis.
5. Blood transfusion or needle prick—this can alert the clinician to look for infections such as hepatitis B.
6. Contact with a jaundiced patient—this can alert the clinician to suspect hepatitis A.
7. Sepsis—umbilical sepsis/intra-abdominal sepsis predispose to infection and fibrosis of biliary tract or portal vein thrombosis.
8. Preceding illness/surgery/hospitalisation.

Treatment History

The clinician should enquire in detail about the treatment given in the present as well as the past

episodes of illness. Any treatment records that are available should be reviewed and relevant findings should be noted. Response to treatment should also be enquired about. The important aspects to be touched while taking the treatment history are as follows:

1. History of hospitalisation
   - Indications for admission
   - Nature of treatment given
   - Duration of stay in hospital
   - Any complications
   - Details of any surgical or invasive intra-abdominal procedures such as laparoscopy, paracentesis, liver biopsy and endoscopy (Table 10.9)
   - Details of any laboratory tests conducted—this may give a clue if the child was normal previously or any disorder was present at that time
2. History of hepatotoxic drugs administered
   - Antibiotics—erythromycin estolate causes cholestasis, jaundice and hepatic dysfunction
   - Antiepileptic drugs—phenytoin, valproic acid
   - Antitubercular drugs—isonicotinylhydrazine (INH)
   - Antipyretic drugs—paracetamol is hepatotoxic. Acetaminophen is metabolised by cytochrome P450 and glutathione to mercapturic acid conjugate. When the hepatic stores of glutathione are depleted, intermediary metabolites are formed which damage the liver cells
   - Sulphonamides
   - Anaesthetic agents—halothane
   - Antimetabolites—6-mercaptopurine, methotrexate
   - Carbon tetrachloride
3. History of blood transfusion
   - Age at first transfusion
   - Indication for transfusion
   - Number of transfusions
   - Frequency of transfusions (interval between subsequent transfusions)
   - Route of transfusion (umbilical or intravenous). Umbilical cord catheterisation predisposes to hepatic damage or infection
   - Details of complications, if any. Risk for hepatitis B infection is more if the blood transfused is not screened
   - Any exchange transfusion with indications
4. History of any native treatment with drugs, toxins or native powders. Many of the ingredients in the indigenously prepared powders are hepatotoxic and may cause or aggravate liver cell injury.

TABLE 10.9 Complications of Various Intra-Abdominal Procedures

Procedures	Complications
Paracentesis	May precipitate liver cell failure in ascites
Liver biopsy	May predispose to liver cell failure in children with cirrhosis
Endoscopic retrograde cholangio pancreatography (ERCP)	Bile tract injury

History of Contact with Communicable Diseases

Contact with a known case of tuberculosis and hepatitis B should be noted. Koch's abdomen is a well-known entity in children.

Antenatal History

- Maternal age at conception—increased maternal age is associated with Down's syndrome, which may present with leukaemia and ileal atresia.
- Immunisation—rubella vaccine given to the girls in the prepubertal age or prior to pregnancy prevents rubella in the mother. Rubella presents as hepatosplenomegaly in the children.
- Intrauterine infections—history of fever with rash (TORCH), or painful retroauriculo-lymphadenopathy, may be suggestive of intrauterine infections in the mother. TORCH and syphilis present with hepatosplenomegaly in the baby.
- History of drug intake (Table 10.10).
- Maternal malnutrition—excess of vitamins A and D is associated with renal defects.

TABLE 10.10 Effects of Various Drugs Taken by the Mother

Drug	Effect on Foetus
Thiazides	Damage to the foetal liver
Oxytoxin	Hyperbilirubinaemia
Acyclovir	GI anomalies

- Irradiation predispose to leukaemia and radiation enteritis in the baby.
- Associated illness—diabetes, hypertension and jaundice. Diabetes in the mother is associated with small left colon syndrome, hyperbilirubinaemia and renal vein thrombosis in the newborn. Antihypertensives such as propranolol cause hyperbilirubinaemia; angiotensin-converting enzyme (ACE) inhibitors are associated with renal dysplasia. Jaundice in the mother may be due to hepatitis virus infection. The baby is likely to contract the infection from the mother, which predisposes to neonatal hepatitis.

Neonatal History

- Low birth weight—congenital rubella syndrome is associated with low birth weight and hepatosplenomegaly.
- Jaundice or kernicterus in the newborn period indicates the possibility of liver disorders such as neonatal hepatitis and EHBA.
- Diarrhoea/dehydration in the neonatal period may indicate the presence of malabsorption disorders and cystic fibrosis.
- Septicaemia, intra-abdominal sepsis and umbilical sepsis are associated with infection in the portal vein, which predispose to development of cirrhosis or portal hypertension at a later age.
- Procedures such as umbilical cord catheterisation in neonatal period may predispose to hepatic damage or infection.

Developmental History

Any delay in the milestones (motor and mental) should be asked. Hepatosplenomegaly with mental retardation may be seen in storage disorders such as mucopolysaccharidosis and glycogen storage disorders.

Nutritional History

Malnutrition may be associated with nutritional cirrhosis. The clinician should obtain a detailed dietary history of the child. Malnutrition disorders such as kwashiorkor may be associated with anasarca. Chronic liver disorders are associated with loss of appetite. Vitamin D deficiency is associated with potbelly due to hypotonia of abdominal muscles.

Family History

Certain inherited and metabolic disorders may be present in other family members. History of similar illness in other family members should be enquired. While taking the family history, the clinician should enquire about the following important aspects:

- Consanguineous marriage—some inherited disorders are more common in a baby born to parents with consanguineous marriage (Table 10.11).
- Jaundice—recent history of jaundice (hepatitis A) in the family can identify the source of infection.
- H/o chronic liver diseases in other family members—familial neonatal hepatitis, Byler's disease (familial progressive intrahepatic cholestasis), Wilson's disease, etc.
- Similar illness at the same time in other family members (e.g., food poisoning).

TABLE 10.11 Various Abdominal Findings Associated with Inherited Disorders

Conditions	Inheritance	Findings in the Abdomen
Cystic fibrosis	Autosomal recessive	Biliary cirrhosis
Mucopolysaccharidoses (except Hunter's syndrome)	Autosomal recessive	Hepatosplenomegaly
Hunter's syndrome	X-linked recessive	Hepatosplenomegaly
Niemann–Pick disease	Autosomal recessive	Hepatosplenomegaly
Gaucher's disease	Autosomal recessive	Cholestasis, hepatosplenomegaly
Gangliosidosis	Autosomal recessive	Hepatosplenomegaly

- History of chronic cough in the family. This can alert the clinician to look for disorders such as tuberculosis, cystic fibrosis and α-1-antitrypsin deficiency.

Socioeconomic History

Many abdominal disorders are influenced by the socioeconomic factors. The clinician should enquire about the following aspects regarding the socioeconomic history:

- Living area per family member.
- Ventilation adequate/inadequate—inadequate ventilation or small area for living predisposes to easy spread of infections within the family members.
- Per capita income and the amount spent on food—less income predisposes for decreased intake and nutritional cirrhosis.
- Water and sanitation facilities—amoebiasis and cholera are common in areas which have poor water and sanitation facilities.
- Factories—the clinician should ask about any factory in the neighbourhood that may be emitting toxic substances. For example, a pencil factory or motor vehicle workshop near the house can lead to lead contamination, which can cause abdominal colic.

GENERAL EXAMINATION

A thorough general examination is very necessary and gives a lot of clues to disorders related to abdomen. A careful general examination is done prior to the actual abdominal examination for the presence of findings, as summarised in Table 10.12.

TABLE 10.12 General Examination Findings to be Observed in an Abdominal Case

Parameters	Clinical Findings and Associated Conditions
Nutritional status	Growth failure and failure to thrive are seen in storage disorders, chronic diarrhoeal disorders, malabsorptive disorders
Consciousness	Altered sensorium in hepatic failure, renal failure Mental retardation in storage disorders such as mucopolysaccharidosis
Colour	Jaundice in liver disorders Pallor in worm infestation and occult blood loss
Hydration	Dehydration in acute gastroenteritis, vomiting or due to inadequate intake
Eyes	Kayser–Fleischer ring in Wilson's disease Uveitis (inflammatory bowel disease) Episceleritis (inflammatory bowel disease)
Mouth	Aphthous ulcers (inflammatory bowel disease)
Chest	Gynaecomastia in liver failure
Hands	Flapping tremors in liver failure, renal failure
Fingers and toes	Clubbing (inflammatory bowel disease)
Nails	White in liver failure
Legs	Pedal oedema in liver failure
Dilated vessels	Spider angioma in liver failure
Lymph nodes	Lymphadenopathy—leukaemia, lymphoma
Purpura/petechiae	Liver disorders, leukaemia, lymphoma, septicaemia
Hair	Loss of hair in liver failure
Bones and joints	Tenderness over mid-point of sternum in leukaemia and lymphoma Arthritis (inflammatory bowel disease)
Skin	Erythema nodosum (inflammatory bowel disease)
Vital signs	Fever is present in infections such as viral hepatitis, abdominal tuberculosis, leptospirosis, leukaemia, lymphoma

EXAMINATION OF ABDOMEN

Examination of abdomen should be done in every patient as it gives a lot of clues for various disorders, which may or may not be directly related to the abdomen. The abdomen is a part of the GI system, the hepatobiliary system and the genitourinary system. As the abdomen is examined, the organs or abnormal structures can be palpated. The shape and other features of abdomen show normal variations. So, careful examination and interpretation is required. Also, one should remember that the position of the organs may vary, for example, ectopic testes and horseshoe kidney.

Regions

Before examining the abdomen, the clinician should be aware of the abdominal regions, that is, the nine

abdominal region and the perineum (considered the tenth region) (Fig. 10.1). The nine abdominal regions are created by the arbitrary division of the abdomen by four imaginary lines:

1. Two vertical lines from the midclavicle on each side.
2. Two horizontal lines—one at the level of L1 vertebra (transpyloric line) and the other at the level of tubercles of iliac crest (interiliac line).

Surface Marking of the Abdominal Organs

One should know the anatomical site of various organs and their normal sizes. This helps in assessing whether the size is normal or if there is any enlargement of organs. Knowledge of surface marking of various organs helps the clinician to know what to look for.

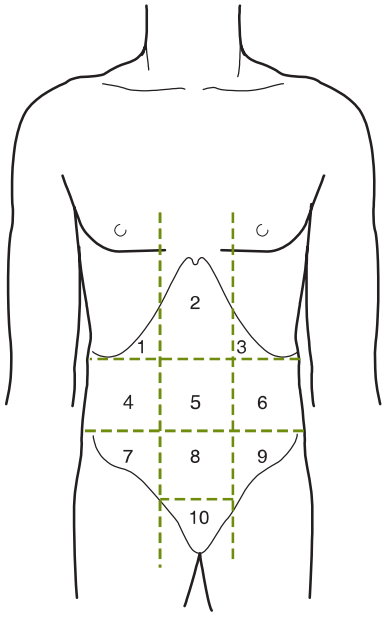


FIGURE 10.1 Abdominal regions. 1 and 3, right and left hypochondrium; 2, epigastrium; 4 and 6, right and left lumbar; 5, umbilical; 7 and 9, right and left iliac; 8, hypogastrium or suprapubic; 10, pubic region.

Inspection

Inspection of abdomen gives a lot of information. External markers of internal diseases can be seen on the abdomen. For instance, dilated vessels are seen around the umbilicus in a patient of portal hypertension. The movements of the intestines can be seen if there is an obstruction in the gut. The movements of abdomen may reflect pathology in the abdomen such as peritonitis or diaphragmatic paralysis. The pre-requisites of inspection are as follows:

- Always stand on the right side of the child to be examined.
- The child should lie flat on the back on a firm bed with the hip flexed. Infants and very small children may be examined on the mother's lap.
- Examine with warm hands in a good light and warm surroundings.

During inspection, the examiner should note the following:

- Shape of the abdomen
- Flanks
- Umbilicus
- Movements of abdomen
- Veins on the abdominal wall
- Visible gastric or intestinal peristaltic movements
- Skin over the abdomen
- Swelling
- Hernial sites (inguinal, femoral, umbilical, epigastric and surgical incisional sites)
- External genitalia

Shape

The normal shape of abdomen varies with age. The examiner should note if the abdomen is protuberant, scaphoid or distended.

- Protuberant abdomen or 'potbelly' is seen as a normal variant up to the age of 5 years. It is also seen in conditions with hypotonia of anterior abdominal wall muscles such as hypocalcaemic rickets. The abdomen in children may appear protuberant due to lumbar lordosis till 11–13 years of age. Hence, this finding should be carefully interpreted.

- Scaphoid abdomen is seen in congenital diaphragmatic hernia and severe malnutrition.
- Abdominal distension may be uniform (Box 10.1) or localised (Box 10.2). Uniform abdominal distension may be iatrogenic (after laparoscopic surgery where air is pushed into the peritoneal cavity before surgery) and may also be seen in hypokalaemia and peritonitis. Localised bulge in the abdomen may be seen in poliomyelitis. It is known as 'phantom hernia'.
- Congenital absence of anterior abdominal wall muscles is seen in prune belly syndrome.

Flanks

Flank is the part of the abdomen that lies at the sides between the costal margin and the ilium. It is usually free and slightly curved inwards in normal children. Fullness of flanks is seen in abdominal distension due to any cause such as ascites.

Umbilicus

The examiner should note the position and appearance of the umbilicus. Any abnormal discharge from the umbilicus or hernia in that area should also be noted.

Position. The normal position of the umbilicus is midway between the xiphisternum and pubic symphysis. Any variation in the position of the umbilicus should alert the examiner to look for the associated conditions. Table 10.13 lists the various different positions of umbilicus and the associated conditions.

Appearance. A normal umbilicus is slightly retracted and inverted. The examiner should note any abnormal appearance of the umbilicus or any protrusion from the umbilical area (Table 10.14 and Fig. 10.2).

Umbilical Hernia. It may be seen normally in some children and may close spontaneously by 2 years. The following conditions are usually associated with umbilical hernia (Fig. 10.3):

- Down's syndrome
- Cretinism
- Hurler's syndrome
- Hunter's syndrome

BOX 10.1 Causes of uniform abdominal distension (5*F*)

- *F*luid—ascites
- *F*latus
- *F*oetus—pregnancy
- *F*at—obesity
- *F*aeces—intestinal obstruction

BOX 10.2 Causes of localised abdominal distension

- Localised ascites
- Large bowel obstruction
- Cyst (ovarian or peritoneal)
- Tumours (e.g., kidney masses, neuroblastoma)
- Foetus in early pregnancy (in adolescents)
- Lower abdomen—distended bladder
- Upper abdomen—organomegaly (liver or spleen)

TABLE 10.13 Positions of Umbilicus and Associated Conditions

Positions of Umbilicus	Associated Condition(s)
Normal position	Normal abdomen Ascites
Displaced down	Mass in the upper quadrant
Displaced above	Mass in the lower quadrant (distended bladder, ovarian mass, pelvic mass)

TABLE 10.14 Abnormal Appearance of Umbilicus and Associated Conditions

Appearance of Umbilicus	Associated Conditions
Inverted	Normal umbilicus Obesity
Everted	Umbilical hernia Ascites
Flushed with surface of the abdomen/flattened	Ascites, abdominal wall oedema
Vertical slit	Ovarian or pelvic tumour
Transverse/horizontal slit/smiling (transversely stretched) umbilicus	Ascites Oedema of anterior abdominal wall
Protrusion of mass with positive cough impulse	Umbilical hernia
Red mass	Umbilical granuloma



FIGURE 10.2 Abdominal distension with transversely slit umbilicus in a case of ascites.



FIGURE 10.3 Umbilical hernia.

- Beckwith–Wiedemann syndrome
- Tense ascites

Umbilical Discharge. The umbilical area gets dry after the cord falls by 7–10 days of life. Any discharge in the umbilical area should be evaluated carefully. Redness around the umbilicus may be seen in infections. The clinician should note if there is any abnormal umbilical discharge (Table 10.15).

Movements

Movements of the abdomen should be noted. In a normal child, all the quadrants of the abdomen move equally with respiration. In peritonitis, there is restriction or absence of abdominal movements. Also note if only a part is moving more than other parts, like in hernia.

Normally, the abdomen rises with each inspiration due to contraction of diaphragm. This is followed by fall during expiration. This process is reversed in diaphragmatic paralysis. Paradoxical movements are seen in such children.

TABLE 10.15 Abnormal Umbilical Discharge and Associated Conditions

Umbilical Discharge	Associated Conditions
Serous	Infection
Blood	Granuloma
Greenish discharge	Patent vitello-intestinal duct (which connects the intestine to the umbilicus) is associated with discharge of bile. In the presence of diarrhoea the bile reaches the umbilicus without much change.
Pus	Infection
Urine	Patent urachus—a remnant of omphalomesenteric duct
Faeces	Patent vitello-intestinal duct

Visible Pulsations

Visible gastric or intestinal pulsations are present when there is obstruction of the gut (Fig. 10.4).

Normally they are not visible over the abdomen. Some causes of visible abdominal pulsations are listed in Table 10.16.

Skin over the Abdomen

The skin over the abdomen should be examined for the presence of any abnormalities. The clinician should examine the skin of the abdomen thoroughly and look for the following changes:



FIGURE 10.4 Visible intestinal peristaltic movements with abdominal distension in a case of obstruction of gut.

TABLE 10.16 Visible Pulsations over the Abdomen with Probable Causes

Nature of Visible Pulsation	Probable Causes
Visible gastric pulsations moving from left to right	Pyloric obstruction
Visible intestinal pulsations (step ladder pattern of peristaltic movements)	Intestinal obstruction in the distal part
Right to left movement	Transverse colon obstruction
Transmitted pulsations	Abdominal aortic pulsations pushing a mass in front of it
Expansile pulsations	Pulsations of aneurysms

- Stretched skin
- Shiny skin
- Scars of previous surgery, ascitic tap, peritoneal dialysis, etc.
- Sinuses
- Striae—purple striae are seen in Cushing's syndrome
- Plasters—these could denote recent procedures such as tapping

Veins on the Abdominal Wall

Usually the veins are not visible on the anterior abdominal wall. They may be visible if there is increased flow in the anterior abdominal wall vessels. The conditions associated with visible dilated veins over the abdomen include

- Portal hypertension (Fig. 10.5)
- Constrictive pericarditis
- Superior vena cava (SVC) obstruction
- Inferior vena cava (IVC) obstruction

If the veins are seen, the following should be noted:

- Dilated/tortuous
- Position of veins in the abdominal wall—anterior/lateral/back

Swelling

The examiner should look for any swelling on the abdomen and note the following features:

- Site, size and shape of the swelling.
- Any increase in size after coughing (cough impulse) or straining.
- Persistent/not persistent.



FIGURE 10.5 Distended superficial abdominal veins in a case of portal hypertension.

- Movements of the swelling—in thin individuals, the peristaltic movements of the intestines may be seen as a mass moving from one place to other.
- Pulsatile/not pulsatile—aneurysms or swellings in front of the aorta are pulsatile.
- Appearance on lying down—a reducible hernia appears on standing but disappears on lying down.

Examination of Hernial Orifices

Hernia is the protrusion of a viscus or a part of viscus through a normal or abnormal opening. The clinician should examine the orifice for swelling, cough impulse, reducibility and compressibility. Hernia in the anterior abdominal wall is the commonest form of hernia. The common sites of hernia are

- Inguinal hernia—protrusion of abdominal contents such as intestine through the inguinal canal. This can be indirect or direct. Indirect hernia is due to herniation into the processus vaginalis. Direct hernia is due to herniation through a weak transversalis fascia.
- Femoral hernia—protrusion of abdominal contents such as intestine through femoral canal.
- Umbilical hernia—protrusion of abdominal content such as intestine through the umbilicus.
- Exomphalos is due to failure of all or a part of the midgut to return to the coelom during the growth of the foetus (Fig. 10.6).
- Epigastric hernia is seen through a defect in the linea alba. The common site is between the umbilicus and the xiphisternum. This is rare in children.



FIGURE 10.6 Exomphalos.

- Incisional sites—incisional hernia is common in obese children, particularly after surgery for infections such as peritonitis.

Examination of Posterior Abdominal Wall

Always examine the posterior abdominal wall for the presence of dilated vessels. Also look for fullness in the renal angles.

Palpation

As the abdomen is not covered by a bony cage, any enlarged organs and other structures can be easily palpated. Hence, palpation of abdomen gives a lot of information. The pre-requisites are as follows:

- The child should lie supine on a firm bed with both the hip joints flexed.
- The child should be asked to take deep breaths.
- The examiner should stand on the right side while the head of the child should be turned towards the left side.
- The hands of the examiner should be warm and dry.
- The examining hands should be moulded according to the area of palpation. They should not be kept rigid. Avoid sudden poking with the fingertips.

It is better to examine in an orderly manner so that important findings are not missed. Start with superficial palpation. This is followed by deep palpation. The examiner should start the palpation from the left iliac fossa and proceed in an anticlockwise direction ending in the suprapubic region unless tenderness is present at any site. If so, then that area is examined in the last and this pattern may not be followed. If palpation is done in this manner, the intra-abdominal structures are examined in the following order:

1. Left kidney
2. Spleen
3. Right kidney
4. Liver
5. Urinary bladder
6. Aorta and para-aortic glands

Finally, the hernial sites and the external genitalia should be examined.

Superficial Palpation

This is done by palpating the abdomen without applying any pressure. The examiner should note the following points during superficial palpation:

- Local temperature.
- Feel of the abdomen—normal abdomen is soft. The abdomen will be tense if there is collection of excessive fluid in the peritoneal cavity.
- Tenderness—tenderness, if present, may be local or diffuse. An area of local tenderness may point towards the possible organ involved, as given in Table 10.17.
- Guarding and rigidity—guarding refers to the voluntary contraction of the anterior abdominal muscles on palpation to guard inflamed organs within the abdomen. Rigidity is abnormal muscle tension or inflexibility of the abdomen. Guarding and rigidity are seen in conditions causing peritoneal inflammation or irritation.
- Divarication of recti—the recti muscles of anterior abdominal wall join in the midline. In divari-

TABLE 10.17 Possible Pathology/Organ Involved According to the Area of Tenderness

Area of Tenderness	Condition/Organ Involved
McBurney's point tenderness	Appendicitis
Tip of ninth costal cartilage on the right side	Gall bladder tenderness in cholecystitis
Epigastric region tenderness	Gastritis
Renal angle tenderness	Renal involvement
Suprapubic tenderness	Bladder involvement

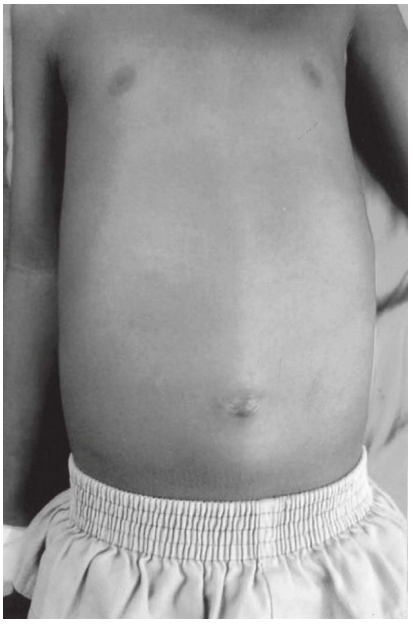


FIGURE 10.7 Divarication of recti in a case of chronic ascites. Note the gap between the recti in the midline.

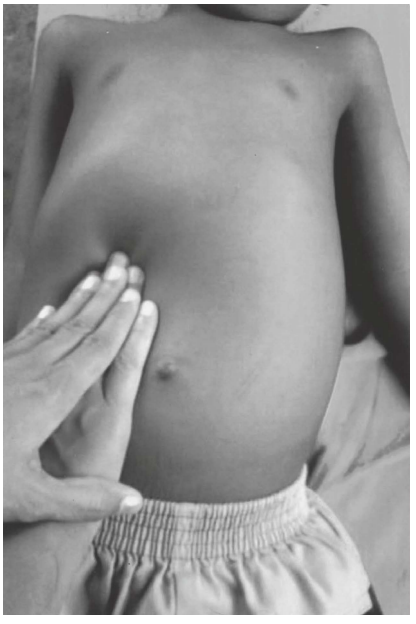


FIGURE 10.8 Dipping method of palpation.

cation of recti, there is a gap in the midline (Fig. 10.7).

- Direction of flow in distended veins, if any. To detect direction of blood flow in the prominent abdominal veins, the examiner should select a long vein on the abdomen without any tributaries. With the patient still in standing position, he should place two fingers over the vein. Then he should apply some pressure on the vein and separate the fingers. This method will empty the vein. One of the fingers should then be released and he should look for the filling of the vein. If there is no filling, he should repeat the procedure but release the other finger and look for the filling of the vein. The direction from which the vein fills gives the direction of blood flow in the vein. The direction of flow in the prominent abdominal veins can help the examiner to diagnose the underlying condition (Table 10.18).

TABLE 10.18 Direction of Blood Flow in Dilated Veins and Associated Conditions

Direction of Blood Flow in Dilated Veins	Condition
Away from umbilicus	Portal hypertension Portal obstruction
From below upwards	IVC obstruction
From above downwards	SVC obstruction

Deep Palpation

Deep palpation is done to look for any organ enlargement, abnormal abdominal mass (e.g., renal mass) or rebound tenderness (Fig. 10.8). Palpation of deep blood vessels (abdominal aorta/femoral vessels) is also done by this method.

Conventional Method. The radial side of the index finger is placed parallel to the border of the organ to be palpated and the organ is palpated by the tip of the fingers. This helps to detect any palpable mass and define its site.

Dipping Method. It is used to palpate abdominal organs in children with tense ascites. The examiner should place the hand flat on the abdomen and make a quick dipping movement so that the fluid is displaced suddenly. The sudden displacement of fluid gives a tapping sensation over the surface of the organ (liver/spleen) similar to a patellar tap. This helps to detect and map the outline of any enlarged abdominal organ.

Rebound Tenderness (Blumberg's Sign). The examiner presses the abdomen firmly with the palm of the hand and then suddenly releases the pressure by moving away the hand. In peritoneal inflammation, this manoeuvre results in severe pain. For instance, in patients with appendicitis, there is rebound tenderness in the right iliac fossa.

Examination of an Abdominal Mass

Site. The site of the mass may give the examiner a clue about the organ involved. Table 10.19 correlates some common sites to the probable organ(s) involved.

Size. The size of the swelling varies according to the size of the organ involved. For instance, gall bladder swelling presents as a small cystic swelling in the right hypochondrium at the tip of the ninth costal cartilage.

TABLE 10.19 Site of the Mass and Probable Organ Involved

Site of Swelling	Probable Organ Involved	Conditions
Right hypochondrium	Liver Gall bladder	Hepatomegaly
Left hypochondrium	Spleen	Splenomegaly
Epigastric region	Left lobe of liver	Hepatomegaly involving left lobe
Right iliac fossa	Appendicular mass Ileocaecal mass	Appendicitis, carcinoid syndrome Intestinal tuberculosis
Left iliac fossa	Colon	Rectal obstruction, fecoliths
Right lumbar region	Right kidney Appendix	Ectopic or unascended kidney Appendicular mass
Left lumbar region	Left fallopian tube, ovaries Left kidney	Tubo-ovarian mass Ectopic or unascended kidney
Around the umbilicus	Mesentery Small intestine	Mesenteric cysts Intussusception
Pubic region	Bladder Uterus	Full bladder, urinary obstruction Uterus in early pregnancy

Shape. Shape of the mass gives a clue about the possible organ involved. For instance, swellings arising from organs such as liver, spleen, kidney and gall bladder usually retain their original shape, whereas swellings arising from the stomach, intestines and peritoneum are distorted in shape. A sausage-shaped mass is seen in intussusception where the proximal portion of intestine invaginates into the distal segment.

Surface. The surface of the mass gives clues about the diagnosis of various clinical conditions.

Surface of the mass	Conditions
Smooth	Mesenteric cysts, loculated ascites, choledochal cyst, ovarian cyst, distended bladder
Irregular	Inflammatory lesions, malignancy
Nodular	Malignancy

Border/Margin. The border of the organ enlarged depends upon the aetiology. An ill-defined swelling indicates an inflammatory pathology whereas a well-defined swelling may denote a neoplasm. Margins of the liver are normally smooth; they are sharp and leafy in cirrhosis.

Skin over the Mass. Note for any ulcer, colour change. Redness is seen over inflammatory swellings. Peau d'orange appearance is seen in lymphatic obstruction. Also, assess the local temperature over the mass. It is increased if the mass is inflamed.

Plane. The swelling may lie in anterior abdominal wall (skin, subcutaneous tissue, abdominal muscles), or may be intra-abdominal (organs in abdomen) or retroperitoneal (kidney).

Terminology	Arise from structures
Parietal swellings	Skin Subcutaneous tissue Abdominal muscles
Intra-abdominal swellings	Non-retroperitoneal intra-abdominal organs Retroperitoneal organs

The examiner can determine the plane (structural depth) of the mass by the following tests:

- Rising test—in supine position, the child is asked to raise the head end. This makes the abdominal muscles taut so that the intra-abdominal swellings become less prominent while the subcutaneous and parietal swellings become more prominent.
- Carnett's test—in supine position, the child is asked to raise the leg end from the bed so that the abdominal muscles become taut. This also makes the subcutaneous and parietal swellings more prominent and the intra-abdominal swellings less prominent.
- The examiner asks the child to blow air with the mouth shut. If the abdominal mass becomes more prominent, the plane is more likely to be parietal, and if it becomes less prominent it is likely to be intra-abdominal.

Other methods for determining the plane of an abdominal mass

Procedure	Inference
When the child is asked to raise the head or legs from a supine position, the swelling becomes more prominent and remains mobile in all directions. The skin over the mass cannot be pinched.	Mass arising from skin
When the child is asked to raise the head from a supine position, the swelling becomes more prominent and remains mobile in all directions. But the skin over the mass can be pinched.	Mass arising from subcutaneous tissue
When the child is asked to raise the head from a supine position, the swelling becomes more prominent and less mobile.	Mass arising from the muscles of anterior abdominal wall
When the child is put in knee–elbow position, the swelling falls forward and is mobile.	Intra-abdominal but not retroperitoneal mass
When the child is put in knee–elbow position, the swelling does not fall forward and is not mobile.	Retroperitoneal mass

Consistency. The swelling may be soft, firm, hard or pleomorphic (variable) in consistency according to the structure involved and the possible pathology. Swelling from kidney and lymph nodes is firm to hard, while that from intestines is soft in consistency (Table 10.20).

In acute conditions, the swelling is soft; in chronic cases, they are firm to hard. Swelling due to infective causes is soft. Hence, consistency often gives a clue to diagnosis.

Tenderness. Tenderness is present in inflammatory or malignant masses.

Mobility. See if the movement of the swelling is independent of respiration. In aneurysm of aorta, the swelling distends with each heartbeat. Swellings arising from liver and gall bladder move with respiration.

The structures arising from the mesentery are mobile in the direction perpendicular to the line of attachment of mesentery. Masses originating from retroperitoneal structures are not mobile.

Pulsations. The pulsations felt over a mass may be transmitted or expansile. This is tested by placing two fingers in approximation over the mass. In a mass with expansile pulsations, the fingers are separated with each pulsation as in aortic aneurysm. If the fingers are not separated, it is called a transmitted pulsation. Such pulsations occur if the mass lies in

TABLE 10.20 Probable Condition/Structure Affected According to Consistency of Mass

Consistency	Probable Condition/Structure Affected
Soft	Cystic swellings such as ovarian cyst, mesenteric cyst, renal, splenic cyst, encysted ascites, full bladder
Firm	Liver, spleen
Hard	Malignancy
Pleomorphic (variable consistency)	Abscess

front of the aorta.

Fluctuation test. When suppuration occurs in a swelling, there will be fluctuation. Fluctuation is seen in cyst-containing fluid.

Reducibility. Press over the swelling and see if it decreases in size. If the swelling is connected to the abdominal cavity, the contents will be displaced and the swelling reduces in size. A swelling due to simple hernia is reducible, while that due to an obstructed hernia is not reducible.

Compressibility. Press over the swelling and note if the swelling is firm or can be compressed. Cystic swellings containing fluid can usually be compressed.

Transillumination. A torch with rubber cuff is placed over a swelling in a dark place. When the light is switched on, the translucency around the torch is observed. In swellings containing clear serous fluid such as hydrocele, the translucency extends for about 2–2.5 cm beyond the cuff.

Pitting. Note whether the mass or swelling is pitting on pressure. In patients with parietal abscess or loaded colon, pressure application with a finger over the mass causes an indentation in the mass.

Palpation of Specific Organs

Liver. Liver size is measured below the right costal margin in midclavicular line by palpation. Liver span refers to the distance between the upper and the lower borders. The lower border is defined by palpation. The upper border is defined by tidal percussion, as described on page 456. Palpation of liver can be done by one of the following two methods:

1. The examiner should place the palm of the hand over the abdomen lateral to the rectus abdominis muscle with the fingers pointing towards the right subcostal region. The child is then asked to take deep breaths. The index and middle fingers of the examiner should be used to palpate the enlarged liver. The enlarged liver will touch the fingers at the height of inspiration. If the liver is not felt, move the hand upwards towards the right subcostal margin till it becomes palpable (Fig. 10.9a).
2. The examiner should place the palm of the hand over the abdomen with the fingers parallel to the right subcostal region (parallel to the border of liver). The palpation should be started from the right iliac fossa. The radial border of the index finger should be used to palpate the enlarged liver. With the hand in place as described, the examiner should ask the child to take a deep breath and the enlarged liver will be felt by the fingers. If it is not felt, he should keep moving the hand upwards till it becomes palpable. However, the examiner should be careful not to start palpation too close to the right costal margin (Fig. 10.9b).

Spleen. A palpable spleen is always abnormal. It has been observed that the spleen should be about three times its normal size to be palpable clinically. The direction of enlargement is towards the right iliac fossa. The size is measured in centimetres from the left costal margin towards the right iliac fossa.

Methods for palpation: Different methods for palpation are used according to the condition and size of the spleen (Table 10.21).

1. The palpation of spleen is usually done with the palm of the right hand with the fingers pointing towards the left subcostal margin. The left hand is kept posterolaterally over the left lower rib cage to support it from below. Palpation should start from the right iliac fossa and move towards the left hypochondrium. The examiner should ask the child to take deep breaths during this procedure. An enlarged spleen can usually be palpated by the tip of the fingers during inspiration. If the spleen is not palpable, the examiner should slowly advance the hand towards the left subcostal margin and repeat

TABLE 10.21 Palpation of Spleen in Various Conditions

Conditions	Palpation Procedure
Mildly enlarged spleen	Patient in right lateral position Hooking method used
Moderately enlarged spleen	Patient supine Palpation from the right iliac fossa
Presence of ascites	Patient in supine position Dipping method used



(a) (b)

FIGURE 10.9 Palpation of liver.

the procedure. A moderately enlarged spleen can usually be palpated with the patient in the supine position by this method (Fig. 10.10).

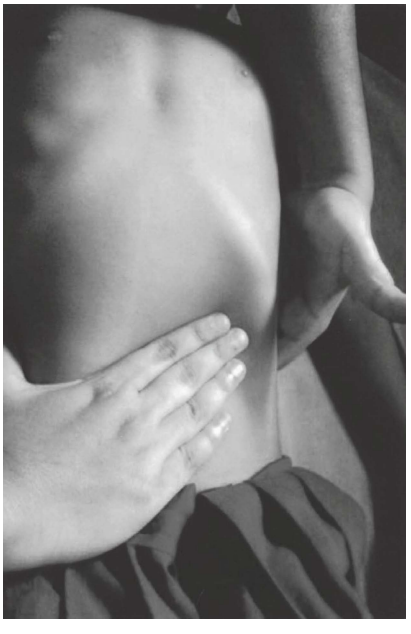


FIGURE 10.10 Method of palpation of spleen.

2. To palpate a mildly enlarged spleen (just palpable spleen), the patient should be put in the right lateral position and the fingers should be insinuated below the left subcostal margin.
3. Hooking method—this is also useful if the spleen is mildly enlarged. In this method, the palpation is done with hooked fingers of the left hand as the patient lies supine. The examiner should stand on the left side facing the foot end of the child. The hooked finger should face the diaphragm while palpating for spleen under the left subcostal region (Fig. 10.11).
4. Dipping method—in the presence of ascites, an enlarged spleen can be palpated by this method. The patient lies in the supine position. Sudden pressure is exerted by the palpating fingers to displace the fluid and palpate any enlarged organ.
5. Middleton's manoeuvre—this is another method of palpation of spleen. The examiner should stand on the left side of the patient facing the foot end of the bed. The spleen is palpated with hooked fingers of one hand around the left costal margin, while the other hand is placed



FIGURE 10.11 Palpation of spleen by hooking method.



FIGURE 10.12 Middleton manoeuvre for palpation of spleen.

on the posterolateral aspect of lower thorax and pressure is exerted. An enlarged spleen can be palpated by the tip of the fingers at the end of the deep inspiration (Fig. 10.12).

Gall Bladder. Gall bladder can be palpated only when it is enlarged. It is palpated as a round, globular mass along the lateral margin of the rectus abdominis muscle at the tip of the ninth costal cartilage on the right side. The gall bladder swelling moves with respiration.

The examiner draws a line from the left anterior superior iliac spine through the umbilicus. This line is then extended further so that it meets the right subcostal margin. The gall bladder lies at the junction of this line and the subcostal margin, provided the shape of the abdomen is normal. The gall bladder is better seen than felt when enlarged.

In children with hepatic enlargement, the gall bladder comes down along with the liver. The upper border merges with the liver.

Kidneys. Kidney swellings are ballotable and hence bimanually palpated (Fig. 10.13). One hand of the examiner is placed posteriorly below the lower ribcage and the other hand is placed anteriorly in the lumbar region. One of the hands is kept fixed and other hand is pushed. The examiner then asks the child to take a deep breath as he uses both his hands to palpate the area. The kidney can usually be palpated between the two hands. The examiner should assess the size, shape, surface and consistency of the kidneys.

The differences between splenic and kidney swelling are listed in Table 10.22.

Percussion

The direction of percussion should be from above



FIGURE 10.13 Examination of kidney by bimanual palpation.

TABLE 10.22 Differences between Splenic and Kidney Mass

Features	Spleen	Kidney
Site	Located anteriorly behind ninth, tenth and eleventh ribs	Located posteriorly in the L_1 vertebral region
Plane	Intra-abdominal	Retroperitoneal
Palpation findings		
Plane of the swelling	Superficial	Deep
Edge	Sharp	Rounded edge
Splenic notch	Notch present	Notch absent
Insinuation of fingers between the costal margin and the organ	Fingers cannot be pushed between spleen and costal margin	Can be insinuated
Bimanual palpation	Bimanually not palpable (huge spleen may be palpable bimanually)	Ballotable
Movement with respiration	Moves freely with respiration	Restricted movement
Direction of enlargement	Enlarged spleen goes towards right iliac fossa	Kidney goes towards respective lumbar fossa
Get above the swelling (palpate the upper end of the swelling)	Not possible	May be possible
Percussion findings		
Band of colonic resonance	Band of colonic resonance absent	Band of colonic resonance present
Examination of loin	Loin free and resonant	Loin full and dull

downwards. The examiner should observe the general note of the abdomen. It is normally resonant.

- Resonant—normally present
- Dull—presence of fluid
- Hyper-resonant—presence of pneumoperitoneum
- Dull in the pubic area—bladder distension

Tidal Percussion

This method helps to differentiate liver dullness from the dullness of pleural effusion. The examiner begins the percussion from the right infraclavicular region and proceeds downwards. Once the liver dullness is reached, the examiner keeps his hand at the same site and asks the patient to take a deep breath. With the patient holding his breath, the percussion is done at the same site again.

If the site becomes resonant, it is inferred that the dullness was due to liver. This is because the liver is pushed down by the expanded lungs in inspiration. In cases with pleural effusion, the dullness persists at the same level.

Fluid Thrill

This method helps to detect free fluid in the abdomen. Ascites can be demonstrated clinically by eliciting for fluid thrill (Fig. 10.14).

The patient is asked to lie in supine position. One hand of the examiner is placed on the flank of the abdomen. The nurse/attendant is asked to place the ulnar side of his/her hand lightly on the middle of the patient's abdomen. It is ensured that the hand on the middle of the abdomen is held lightly because firm pressure can prevent transmission of the thrill.

The examiner then gently taps the other side of the abdomen and feels the sensation by the other hand placed on the flank. If free fluid is present in the abdomen, a fluid thrill is appreciated on the opposite side of the tapping hand.



FIGURE 10.14 Method to demonstrate fluid thrill.

Liver Span

Liver span is measured to delineate the extent of liver and to detect upward enlargement of the liver (seen in amoebic liver abscess). The examiner begins the percussion from the second intercostal space in the right midclavicular line and proceeds downwards. The intercostal space in which dullness starts is noted. The length between this point and the lower border of the liver along the midclavicular line is measured to give the liver span. The liver span varies with age (Table 10.23). In the presence of right-sided pleural effusion or empyema, there can be a false impression of hepatomegaly. This can be confirmed by tidal percussion (described earlier in this chapter).

TABLE 10.23 Age-Wise Variation of Liver Span

Age	Liver Span (cm)
Birth	5.6–5.9
2 months	5
1 year	6
2 years	6.5
3 years	7
4 years	7.5
5 years	8
6–12 years	9
Adolescents	8–10 in girls 10–12 in boys

Shifting Dullness

This is a method to detect free fluid in abdomen. However, it can be demonstrated only if about 1000 mL of fluid is present in the peritoneal cavity in case of older children and adults. In younger children, it can be positive even with a lower amount of fluid.

First, the child is percussed for bladder dullness (Fig. 10.15a). The abdomen is then percussed from the midline to the lateral side. Normally flanks are resonant. In the presence of ascitic fluid, there is dullness in flanks. Once the dullness is noted, the plexiometer finger is fixed on the abdomen. The patient is then asked to turn laterally to the opposite side (Fig. 10.15b). After about a minute, the same area is percussed again.

If shifting free fluid is present, the previously dull area becomes resonant. Additionally, the area on the opposite side that was resonant previously becomes dull.



(a)



(b)

FIGURE 10.15 Method to demonstrate shifting dullness in a case with ascites.

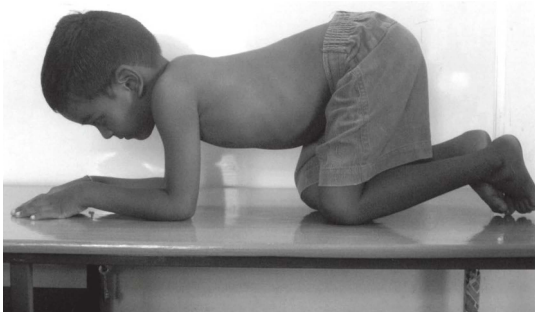


FIGURE 10.16 Knee-elbow position for puddle sign.

Puddle Sign

This method can clinically detect even 50 mL of fluid in the peritoneal cavity.

The patient is put in knee–elbow position for 5 minutes and the fluid is allowed to accumulate in the umbilical area (Fig. 10.16). With the patient still in the same position, the examiner percusses near the umbilicus and in the surrounding dependent part of the abdomen. A dull note is noted even if minimal ascites is present. The same patient may have a tympanitic (resonant) note when the abdomen is percussed in supine position.

Auscultation

The abdomen should be auscultated with a stethoscope to find out abnormalities in blood flow or bowel movements.

Bowel Sounds

The examiner should auscultate the abdomen for bowel sounds by placing the stethoscope in the right iliac fossa. The bowel sounds are best heard in this area because of the turbulence created due to the ileocaecal valve. These may be normal, increased or decreased in intensity and frequency.

The normal bowel sounds are metallic in nature with a tinkling quality while the abnormal bowel sounds are high pitched and loud. The frequency of normal bowel sounds is given in Table 10.24. They can be increased or decreased (Table 10.25).

TABLE 10.24 Normal Bowel Sound Frequency

Region	Frequency (per minute)
Small bowel	10–15
Large intestine	3–5

TABLE 10.25 Abnormal Bowel Sound Frequency

Bowel Sounds	Conditions
Increased	Intestinal obstruction Hyperthyroidism Diarrhoea
Decreased/absent	Peritonitis Hypokalaemia Paralytic ileus

Other Abnormal Sounds

Other abnormal auscultatory findings in the abdomen are as follows:

1. Bruit over the liver—it is caused by turbulence of blood flow and is seen in
   - aortic aneurysm,
   - haemangioma liver and
   - coeliac artery stenosis.
2. Friction rub—this may be found in
   - hepatic area (in perihepatitis) and
   - splenic area (in perisplenitis).
3. Venous hum—this is heard over the collaterals due to portosystemic shunts between the patent umbilical vein and portal vein.
4. Cruveilhier–Baumgarten syndrome—this is characterised by a loud venous hum due to increased blood flow through the recanalised umbilical vein.

Auscultation with Palpation and/or Percussion

Auscultation may be combined with palpation and percussion for clinical assessment of several conditions.

Auscultopercussion. This is a combination of auscultation and percussion. It is used to detect minimal ascites.

The child should be put in a knee–elbow position for a few minutes to allow the fluid to collect around the umbilicus. The examiner should then place the diaphragm of the stethoscope over the umbilicus and start percussing away from the umbilicus. There is a change in the auscultatory tone once the percussion crosses the fluid level. This test can also

be done by scratching the abdominal wall away from the umbilicus and observing the point where the auscultatory note changes.

Succussion Splash. Succussion splash occurs when there is a collection of air and fluid. It can be elicited by clinical observation, palpation and auscultation.

The patient should be asked to lie in supine position. The examiner should then roll the patient from side to side to agitate the fluid or gas present in the cavity of the stomach or dilated intestine. A splashing noise is heard clinically. Even on palpation, a thrill is felt. This sound can also be observed by auscultation over the fluid-filled cavity.

Succussion splash may be present in the following conditions:

- Pyloric stenosis
- Intestinal obstruction
- Paralytic ileus
- Prolonged gastric emptying time
- Normal stomach immediately after food intake

Measurement of Abdomen

- Abdominal girth—this should be measured at the umbilical level using a measuring tape. It is important to assess the progress of ascites.
- Spinoumbilical measurement—this is the distance between the umbilicus and the anterior–superior iliac spine. It is measured bilaterally and compared. In normal children, the measurements on both the sides are equal. In unilateral masses, the distance is more on the affected side.

Examination of External Genitalia

Examination of external genitalia is often missed in children. It is important to examine the external genitalia while examining abdomen as many disorders such as cirrhosis, nephrotic syndrome and adrenal tumours are associated with abnormal findings in the external genitalia.

Pre-Requisites

- Before examining the genitalia, the child should be told about the purpose of examination, if the child is able to understand. Or else, the parents or the guardian should be explained about the examination.
- It is important to have a female nurse by the side while examining a female child.
- The child should be asked to empty the bladder prior to examination.
- The room should be well lighted.

Position

An older child may be examined in frog position, lithotomy position or knee–chest position. A small child may be examined on the mother's lap.

Findings

During the examination of genitalia, the clinician should look for the following:

- Gender of the baby—external genitals develop from two genital tubercles and one genital swelling. Depending on the presence or absence of testosterone, external genitalia differentiate into male or female genitalia. Hence, any abnormality of this hormone results in genital abnormalities.
- Ambiguous genitalia—in female babies with congenital adrenal hyperplasia, clitoromegaly is present. It gives the impression of a penis. In male babies with decreased testosterone level or end organ insensitivity, the penis may not develop properly. Hence, assessment of sex becomes difficult in such cases. In certain cases, it is difficult to assess the gender by external examination. The gender in such cases with ambiguous genitalia should be confirmed by chromosomal studies.
- Secondary sexual characters—the presence or absence of pubic hair helps in sexual maturity rating in adolescence. Absence of pubic hair and loss of secondary sexual characters is seen in liver failure.

Examination in Males

- Testis—note if the testes are bilaterally present, and normal in size and position. Testicular atrophy is seen in cirrhosis or liver failure. Testes may be abnormally placed (Table 10.26). Various complications occur in undescended and ectopic testes (Box 10.3). Also examine the genitalia for any obvious swelling and tenderness (Table 10.27).

TABLE 10.26 Position of Testes in Various Clinical Conditions

Conditions	Position of Testes
Undescended testis	The testis lies in its normal path of descent but does not reach the scrotum. It may be present in the abdomen, inguinal canal or superficial inguinal pouch in the inguinal region.
Ectopic testis	The testis lies out of its normal path of descent. It may be present in the abdomen, femoral canal.
Retractile testis	The testis lies in the inguinal region but can be pulled down to the scrotum.

BOX 10.3 Complications of undescended and ectopic testes

T	Torsion
E	Epididymo-orchitis
S	Sterility
T	Trauma (more prone for trauma). Recurrent trauma may result in atrophy
I	Inguinal hernia, indirect Interstitial hernia
S	Seminoma

TABLE 10.27 Disorders That Can Manifest in the External Genitalia

Clinical Findings	Disorders
Testicular atrophy	Cirrhosis
Tender, enlarged testis	Acute epididymo-orchitis/torsion of testis
Painless, enlarged testis	Malignancy
Scrotal swelling	Hydrocele, hernia
Varicocele of pampiniform plexus	Obstruction of testicular veins (commonly of the left side), hypernephroma

- Penis—note the size and shape. In chordee, the shaft of the penis is curved due to fixed bending. It may be associated with hypospadias or epispadias. Micropenis is seen if there is any chromosomal defect.
- Priapism is a condition where there is thrombosis in the prostatic venous plexus; the penis remains erect and is painful. This may be seen in children with conditions predisposing to thrombosis such as leukaemia or sickle cell anaemia. It is also seen in spinal cord diseases.
- External urethral orifice—note if the site of the urethral meatus is normal in position or situated ventrally (hypospadias) or dorsally (epispadias). Look for meatal stenosis. Do not retract the skin forcibly. The presence of phimosis is normal in infancy. Phimosis is associated with long foreskin, which may bulge out during micturition. Also, urinary stream will be thin and weak. There will be narrowing of prepuce. If it persists after 2 years, or if it is associated with symptoms such as obstruction to urinary flow, surgical intervention is considered. Paraphimosis is a painful condition where the tight prepuce is retracted but cannot be returned to its normal position.
- Scrotal oedema.

Examination in Females

The examiner should look for the following features in females:

- Vaginal bleeding—it is normal in newborns due to withdrawal of maternal hormones after clamping of the umbilical cord.
- Vaginal discharge—occurs in normal children about 6 months before puberty and in vulvovaginitis.
- Vulval oedema—nephrotic syndrome.
- Clitoromegaly—congenital adrenal hyperplasia.

Rectal Examination

Rectal examination is important in children with anorectal anomalies. It helps to differentiate between congenital and acquired megacolon. In congenital megacolon, the rectum is empty, whereas in acquired megacolon, the rectum is loaded with stools.

Examining Finger Specifications

For rectal examination in newborns and infants, the examiner should use the little finger. In older children, the index finger can be used for rectal examination.

Position of the Patient

The child should be asked to lie in the left lateral position with the thighs flexed over the hips and the knees drawn up.

TABLE 10.28 Structures Palpated by Rectal Examination

Direction of Palpation	Structures Palpated
Anteriorly	Rectovesical pouch and seminal vesicles, prostate can be palpated for the presence of any pathology. In females the cervix can be palpated anteriorly.
Laterally	The side walls of the rectum should be palpated and it is possible to reach up to the side walls of the pelvis.
Posteriorly	The hollow of the sacrum and the coccyx can be felt.

Procedure

The examiner should lubricate the gloved hand and stand behind the patient facing the patient's feet. The pulp of the finger should be placed flat on the anus so that the volar aspect of the finger is placed on the anus. The examiner should then press firmly at the tip of the anus without flexing the finger so that it enters the rectum. If there is any pain, the rectal examination should be stopped.

With the finger inside the rectum, the examiner should feel for any abnormalities in the rectal cavity or in the walls of the rectum. The finger should be rotated through 360° to examine all parts of the rectum (Table 10.28). Then, it should be brought to the anorectal area to feel for the contraction of the external sphincter muscle. This can be felt as a reflex contraction or by asking the patient to contract the sphincter voluntarily.

HEPATOMEGALY

Hepatomegaly refers to enlargement of liver. The basic aspects of the liver are discussed in Box 10.4. Hepatomegaly is common in children. The mechanism of hepatomegaly depends on the aetiological factors (Table 10.29 and Fig. 10.17). Points to be noted in clinical examination in a case of hepatomegaly are given in Box 10.5. While palpating the liver mass, one should look for the following findings:

- Size/liver span
- Edge/margin

BOX 10.4 Liver

The liver has a good functional reserve and considerable ability to regenerate.

Surface marking of the liver:

- Upper border—fourth intercostal space in the midclavicular line.
- Lower border—ninth intercostal space in the midclavicular line.
- Lateral border—sixth rib in the midaxillary line.

Functions of liver

The liver is the main site for synthesis, degradation and regulation in pathways involving carbohydrates, proteins, lipids, trace elements and vitamin metabolism. The functions of the liver are as follows:

- Synthetic—albumin (protein synthesis), gluconeogenesis (using amino acids), coagulation factors (II, V, VII, IX, X) and protein C, S and antithrombin.
- Metabolism—sugar (gluconeogenesis), fat and protein (deamination of amino acids, regulates supply of amino acid to the muscles).
- Excretion—bilirubin.
- Detoxification—drugs (short-acting barbiturates) and hormones (oestrogens).
- Storage—vitamin A (in Ito cells) which lasts for 6 months, vitamin B_{12}, glycogen reserve, iron and copper.
- Secretory—bile secreted by liver makes the digested fat soluble. This promotes the absorption of fat.
- Protective—reticuloendothelial system (Kupffer cells) helps in destruction of bacteria.
- Miscellaneous—production of heat.

Blood supply

The liver has a dual blood supply, that is, from portal vein and hepatic arteries. Portal vein carries blood from spleen, GIT and associated organs. Hepatic arteries also supply blood to the liver. Oxygen is supplied from both sources; approximately, 50% of liver's oxygen demand is met by the portal vein and rest by the hepatic arteries.

TABLE 10.29 Causes of Hepatomegaly

Classification	Causes
Inflammation	Hepatocyte enlarged • Viral hepatitis • Neonatal hepatitis • TORCH • Drug induced hepatitis
	Kupffer cell hyperplasia • Infection • Hypervitaminosis A
	Autoimmune • Chronic active hepatitis • Systemic lupus erythematosus
Congestive	CCF Budd–Chiari syndrome Veno-occlusive disease
Haematological	Extramedullary haemtopoiesis
Infiltration	Erythroblastosis foetalis Haemochromatosis
Malignancy	Primary tumours—hepatoblastoma, hepatocellular carcinoma Secondaries liver Leukaemia Lymphoma
Storage disorders	Fat • Malnutrition—kwashiorkor, obesity, cystic fibrosis • Hyperalimentation
	Glycogen • Glycogen storage disorder
	Lipid • Gaucher's disease • Niemann–Pick disease
	Miscellaneous • Amyloidosis • Mucopolysaccharidosis
Metabolic	α-1-Antitrypsin deficiency Wilson's disease
Increase in vascular space	Intrahepatic obstruction • Hepatic vein thrombosis, veno-occlusive disease • Budd–Chiari syndrome
	Suprahepatic obstruction • CCF, constrictive pericarditis cardiac tamponade
Increase in biliary space	Congenital hepatic fibrosis Extrahepatic obstruction Caroli's disease
Miscellaneous	Hydatid cyst Congenital cysts Haemangioma Vitamin A toxicity (proliferation of ITO cells)

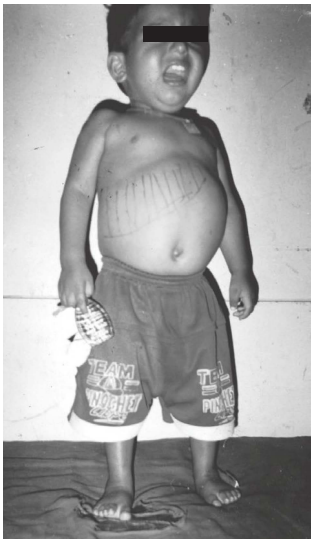


FIGURE 10.17 Hepatomegaly in a child with glycogen storage disease.

BOX 10.5 Clinical examination in a case of hepatomegaly

The following findings give clues to the cause of hepatomegaly:

- Hair—flag sign (kwashiorkor)
- Head—microcephaly (congenital rubella syndrome), hydrocephalus (toxoplasmosis), craniotabes (hypervitaminosis A)
- Eyes—jaundice, Kayser–Fleischer (KF) rings (Wilson's disease), cataracts (Wilson's disease, galactosaemia), hazy cornea (Hurler's syndrome)
- Neck—engorged neck veins, raised jugular venous pulse in constrictive pericarditis
- Chest—spider naevi and gynaecomastia (liver failure)
- External genitals—testicular atrophy
- Skin—scratch marks in cholestasis and biliary obstruction
- Abdomen—splenomegaly in infections like malaria, kala azar, storage diseases, haemolytic anaemia, haematological malignancies and congenital hepatic fibrosis
- Nervous system—tremors and dystonia (Wilson's disease), mental retardation (glycogen storage disorder)
- Skeletal system—rickets (cystinosis, tyrosinosis)

- Surface
- Consistency
- Tenderness
- Pulsations and bruit
- Palpable hepatic rub

SIZE/LIVER SPAN

Liver size refers to the degree of extension below the right costal margin. It is usually measured in centimetres palpable below the right costal margin in midclavicular line.

Liver span is measured by percussing the liver for upper border and palpating for lower border in midclavicular line below the costal margin. Normally, the upper border is situated in the right fifth intercostal space. Upward enlargement occurs in amoebic liver abscess. To judge hepatomegaly, one should know the normal liver span at different ages (Table 10.23).

Hepatomegaly can be classified as mild, moderate or massive on the basis of enlargement below the right subcostal margin (Table 10.30). Liver size should be considered normal in the following conditions:

- Newborn—<2 cm below the right costal margin, consistency soft.
- Older children—approximately 1 cm below the right costal margin, consistency soft.
- Pushed down liver—as in asthmatics, emphysema, pleural effusion, subdiaphragmatic abscess, empyema, pneumothorax, etc. In these conditions, the liver span is normal.
- Visceroptosis—due to lax ligaments.

EDGE/MARGIN

Palpation of edge can give the clue of condition causing hepatomegaly. The edge may be sharp or irregular in cirrhosis. It may be rounded with soft consistency in nutritional deficiency (kwashiorkor).

TABLE 10.30 Grades of Hepatomegaly

Grade	Enlargement Below the Right Subcostal Margin (cm)
Mild	<4
Moderate	5–7
Massive	>7

TABLE 10.31 Surface of Liver in Hepatomegaly

Surface	Congestive Causes
Smooth	Congestive causes
Irregular	Granular (fine irregular) • Portal cirrhosis
	Nodular(coarse irregular) • Postnecrotic cirrhosis • Neoplasms—hepatoma, secondaries liver
Uneven	Multiple hydatid cysts Multiple liver abscess

SURFACE

It also helps in establishing the cause of hepatomegaly, as summarised in Table 10.31.

CONSISTENCY

- Soft—CCF, infective hepatitis (acute and subacute conditions), anaemia, fatty liver, leukaemia, septicaemia, push down livers as in pneumothorax.
- Firm—chronic active hepatitis, cirrhosis, chronic malaria, Koch's infection, chronic kala azar, metabolic conditions (e.g., Wilson's, galactosaemia, tyrosinaemia), chronic amoebic abscess, neonatal hepatitis, lymphoma.
- Hard—congenital hepatic fibrosis, macronodular cirrhosis, chronic myeloid leukaemia, hepatoma, hepatoblastoma, secondaries in liver.
- Cystic—haemangioma.
- Pleomorphic—abscess.

TENDERNESS

Tender hepatomegaly is seen in acute enlargement of the liver due to stretching of Glisson's capsule. In cirrhosis or malignancy, the liver may not be tender unless the capsule is infiltrated. Tenderness may be diffuse or localised (abscess, infected cyst), depending on the extent of involvement. The causes of tender hepatomegaly are given in Table 10.32.

TABLE 10.32 Causes of Tender Hepatomegaly

Classification	Causes
Infections	Viral hepatitis Leptospirosis Infectious mononucleosis Pyaemic liver abscess Amoebiasis Perihepatitis Actinomycosis
Congestive	CCF Acute Budd–Chiari syndrome
Malignancy	Primary malignancy—hepatoma Secondaries in liver after infiltration of the liver capsule
Trauma	Postinvasive procedure (liver biopsy) leading to haematoma or haematobilia
Miscellaneous	Hydatid cyst—infected

PULSATIONS AND BRUIT

A-V malformations are pulsatile. Liver is pulsatile in tricuspid regurgitation (systolic pulsations), tricuspid stenosis and aortic regurgitation (Rosenbach's sign). The pulsations are presystolic in tricuspid stenosis, constrictive pericarditis and pulmonary stenosis. Hepatic bruits are due to blood flow in the liver. They are heard in vascular abnormalities and tumours.

PALPABLE RUB

Thrill or palpable rub over the hepatic area is seen in perihepatitis, after liver biopsy, and malignancy liver after infiltration of the liver capsule.

Some of the liver changes apparent on palpation and their associated conditions are given in Table 10.33.

TABLE 10.33 Liver Palpation Findings in Certain Conditions

Palpation Features	Associated Conditions
Soft, smooth, tender, enlarged liver	Acute CCF Acute viral hepatitis
Firm and nodular liver	Obstructive jaundice Cirrhosis of liver Chronic CCF
Nodular liver	Liver secondaries Hepatoma
Pulsatile liver	Systolic pulsations—tricuspid regurgitation Diastolic pulsations—tricuspid stenosis
Riedel's lobe (a normal variant)	Tongue-like projection of right lobe of liver

SPLENOMEGALY

Splenomegaly refers to enlargement of spleen beyond its normal size. The surface anatomy and functions of spleen are given in Box 10.6. A spleen is said to be significantly enlarged *(significant splenomegaly)* if it is palpable at least 1 cm below the costal margin in a child more than 6 months of age. However in about 30% of newborns and in 15% of infants below 6 months, a palpable spleen is a normal variant.

BOX 10.6 Spleen

It is the largest lymphoid organ. It is situated behind the ninth to eleventh ribs in the left hypochondrium.

Functions

1. Reservoir for platelets, factor VIII, monocytes, erythrocytes and leucocytes.
2. Haematopoiesis in foetus.
3. Repair and destruction of red blood cells (RBCs) by pitting and culling. Pitting removes the intraerythrocytic inclusions such as Howell–Jolly bodies and Heinz bodies. without destroying the RBCs. Culling is the process of removal of damaged, senescent and abnormal RBCs from the circulation.
4. Immune functions—immunoglobulin M (IgM), properdin and tuftsin are produced by the spleen. Spleen destroys the bacteria entering the blood circulation. In children, spleen plays an important role in preventing infections especially by capsulated organisms such as pneumococci. Macrophages present in the spleen play an important role in phagocytosis.

CAUSES

The causes of splenomegaly are as follows:

1. Infectious causes
   (a) Viral—infectious mononucleosis, viral hepatitis, cytomegalovirus (CMV)

infection
   (b) Bacterial—typhoid, infective endocarditis, tuberculosis, meningococcal septicaemia
   (c) Protozoal—malaria, toxoplasmosis, kala azar, trypanosomiasis
   (d) Fungal—histoplasmosis
   (e) Parasitic—hydatid cyst
2. Haematological causes
   (a) Haemolytic disorders
      - Thalassaemia
      - Other haemolytic anaemias
   (b) Extramedullary haemopoiesis
      - Osteopetrosis
      - Bone marrow infiltration
      - Myelofibrosis
3. Congestive causes
   (a) Portal hypertension
      - Extrahepatic—due to hepatic, portal or splenic vein obstruction
      - Intrahepatic—due to cirrhosis of liver
   (b) Congestive cardiac failure
   (c) Constrictive pericarditis
   (d) Budd–Chiari syndrome
4. Disorders of immune regulation—myelofibrosis, combined variable immunodeficiency
5. Infiltrative diseases of spleen
   (a) Lipidosis
      - Gaucher's disease
      - Niemann–Pick disease
      - Gangliosidosis GM1 type 1
   (b) Histiocytosis X
   (c) Myelofibrosis
   (d) Amyloidosis
   (e) Lysosomal storage diseases
      - Cystinosis
      - Mucolipidosis
      - Mucopolysaccharidosis
6. Neoplasms
   (a) Benign
      - Haemangioma
      - Hamartoma
   (b) Malignant
      - Leukaemia
      - Lymphoma
      - Secondaries
7. Connective tissue disorders
   - Juvenile rheumatoid arthritis (JRA)
   - Systemic lupus erythematosus (SLE)
8. Miscellaneous
   - Cyst—congenital, hydatid cyst
   - Sarcoidosis

GRADING

Splenomegaly can be graded, according to the size of spleen, into the following categories:

Hackett's semiquantitative assessment

Grade	Class	Palpation findings
	0	Spleen not palpable even on deep inspiration.
Mild splenomegaly	1	Spleen palpable below costal margin, usually on deep inspiration.
	2	Spleen palpable, but not beyond a horizontal line half way between the costal margin and umbilicus, measured in a line dropped vertically from the left nipple.
Moderate splenomegaly	3	Spleen palpable more than half way to umbilicus, but not below a line horizontally running through it.
Massive splenomegaly	4	Palpable below umbilicus but not below a horizontal line half way between umbilicus and pubic symphysis.
	5	Extending lower than class 4.

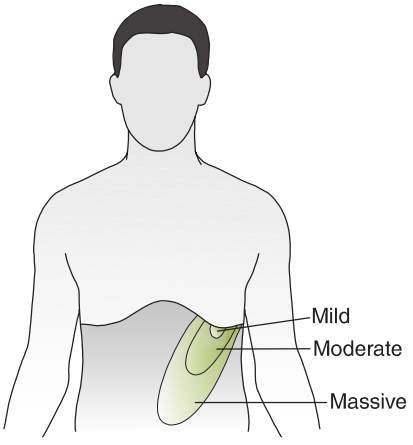


FIGURE 10.18 Grading of splenomegaly.

Splenomegaly is also graded according to the size of spleen palpable below the left costal margin (Fig. 10.18).

Grading	Palpable spleen below the left costal margin (cm)
Mild	<3
Moderate	4–7
Massive	>7

Mild Splenomegaly

The spleen is just palpable or up to 3 cm below the left costal margin. It is associated with the following conditions:

- Acute, subacute or chronic infections such as malaria, typhoid, septicaemia military tuberculosis, leptospirosis, HIV, any viral illness or infective endocarditis
- Congestive cardiac failure
- Portal hypertension (early stage)
- Iron deficiency anaemia
- Acquired haemolytic anaemia
- Acute leukaemia
- Hereditary spherocytosis
- Idiopathic thrombocytopenic purpura (ITP)
- JRA
- Hyperthyroidism

(Conditions associated with moderate and severe splenomegaly may also present with mild splenomegaly in early stages of presentation or after treatment.)

Moderate Splenomegaly

The spleen is about 4–7 cm enlarged (up to the umbilicus). It is associated with the following conditions:

- Viral hepatitis
- Malignant lymphoma
- Acute leukaemia
- Portal hypertension with congestive splenomegaly
- Chronic haemolytic anaemias such as thalassaemia trait
- Malaria, kala azar
- AIDS
- Polycythaemia vera
- Reticulosis
- Amyloidosis

Massive Splenomegaly with Minimal Hepatomegaly

The spleen is enlarged more than 7 cm. It may be associated with the following conditions:

- Portal hypertension due to extrahepatic portal obstruction (EHPO)
- Cirrhosis
- Chronic myeloid leukaemia (CML)
- Chronic haemolytic disease or haemolytic anaemia—thalassaemia major, elliptocytosis and spherocytosis
- Storage disorders such as adult Gaucher's disease and Niemann–Pick disease
- Tropical splenomegaly syndrome—chronic malaria
- Kala azar
- Amyloidosis
- Idiopathic myelofibrosis and myelosclerosis
- Splenic cyst (hydatid cyst) or tumour

CLINICAL ASSESSMENT

The points to be noted in assessment of splenomegaly include the following:

1. Size and degree of enlargement—the spleen usually enlarges towards the right iliac fossa.

Enlargement of spleen is measured as the child breathes deeply. The measurement is taken along the splenic axis from a point on the left costal margin in the midclavicular line to the tip of the enlarged spleen.

2. Margin—splenic notch is usually felt on the anterior border and has a sharp margin. This helps to differentiate splenomegaly from swelling of left kidney where the splenic notch is not present and the margin is rounded.
3. Consistency—the consistency may be soft, firm or hard.
   (a) Soft spleen
      - Enteric fever
      - Septicaemia
      - Normal variant
      - Viral infections—infectious mononucleosis

   (b) Firm spleen
      - Cirrhosis
      - Leukaemia
      - Lymphomas
      - Chronic malaria
      - Storage disorders

   (c) Hard spleen—secondaries
4. Tenderness—the presence or absence of tenderness may help detect the underlying cause of splenomegaly. Tender splenomegaly is found in the following conditions:
   (a) Infective endocarditis
   (b) Splenic infarction
   (c) Splenic abscess
5. Surface—smooth or irregular
   (a) Smooth surface is seen in congestive cases such as portal hypertension.
   (b) Irregular surface is present in hydatid cyst.
6. Movement with respiration—spleen moves downwards and medially during inspiration.
7. Insinuation of fingers—fingers cannot be insinuated between the enlarged spleen and the left costal margin.
8. Palpable rub—splenic rub may be palpable in splenitis.
9. The splenic enlargement must be differentiated from kidney enlargement. The following points are helpful in differentiating spleen from kidney enlargement:
   (a) Kidney is always bimanually palpable or ballotable.
   (b) Splenic notch is felt in splenomegaly.

PSEUDOSPLENOMEGALY

Pseudosplenomegaly refers to the apparent perception of splenomegaly without it actually being present. It may be seen in the following conditions:

- Abnormally elongated mesenteric connections may produce a wandering or proptotic spleen.
- An enlarged left lobe of the liver or a left upper quadrant mass may be mistaken for splenomegaly.
- Spleen may be pushed down as in emphysema of left lung.
- Visceroptosis due to lax ligaments.

SPECIFIC TYPES OF SPLENOMEGALY

Congestive Splenomegaly (Banti Syndrome)

Congestive splenomegaly may result from obstruction in the hepatic, portal or splenic veins. It is associated with the following conditions:

- Wilson's disease
- Galactosaemia
- α-1-Antitrypsin deficiency
- Congenital abnormalities of the portal or splenic veins
- Sickle cell anaemia—the congestive splenomegaly is due to splenic venous obstruction by accumulation of masses of sickled erythrocytes
- Septic omphalitis or umbilical venous catheterisation in newborn babies may also result in secondary obliteration of the portal vein
- Biliary atresia

Hepatic inflammation, fibrosis and vascular obstruction may be seen in the first three

conditions.

Treatment

1. Splenectomy—if hypersplenism is present.
2. Portacaval shunting—usually end-side portacaval shunt decompresses the splanchnic circulation.
   (a) The following criteria should be present before doing this surgery:
      - Adequate liver functions
      - Serum bilirubin not elevated >17 mmol/L
      - Serum albumin >3 g/dL
      - Patent portal vein

   (b) Indications
      - Portal hypertension not responding to medical management
      - Life-threatening haemorrhages from oesophageal varices not controlled by treatment

   (c) Complications
      - Hyperammonaemia
      - Venous deprivation of liver
      - Deterioration of liver function
      - Hepatic encephalopathy
3. Splenorenal shunting—it is not preferred in young children.

Tropical Splenomegaly

Tropical splenomegaly or hyper-reactive malarial splenomegaly is seen in endemic areas where recurrent infection with malarial parasite is common. It is characterised by massive splenomegaly in the absence of parasitaemia.

Pathogenesis

There is an abnormal immune response in malnourished children. Malarial antigens activate B lymphocytes which lead to increased IgM production. Spleen enlarges in an attempt to remove the excess high molecular immune complexes.

Clinical Features

- Massive splenomegaly not decreased with routine antimalarial treatment.
- Features of hypersplenism such as anaemia and bleeding due to thrombocytopenia.

WHO Criteria

The World Health Organisation (WHO) has given several major and minor criteria for tropical splenomegaly. These are given in Table 10.34.

Investigations

- Red blood cells—decreased
- Platelet count—decreased
- Antimalarial antibodies—elevated. Serum IgM levels are elevated
- Smear for malarial parasite—usually negative
- Liver biopsy—sinusoidal lymphocytic infiltration

Treatment

Prolonged course of antimalarials removes the antigenic stimulus due to repeated infection. This enables the immune system to return to normal.

- Tablet chloroquine 10 mg/kg base. This can be used for several months up to 1 year.
- Tablet primaquine 0.3 mg/kg base for 14 days.
- Tablet mefloquine 15 mg/kg in two divided doses.

Prognosis

Splenomegaly improves in about 3 months.

Felty's Syndrome

Splenomegaly is associated with rheumatoid arthritis and neutropenia.

TABLE 10.34 WHO Criteria for Tropical Splenomegaly

Major	Minor
Gross splenomegaly	Hepatic sinusoidal lymphocytosis and Kupffer cell hyperplasia
Immunity to malaria	Normal cellular and humoural immune response to antigenic challenge
Serum IgM elevated	Normal phyto-haemagglutination
Clinical and immunological response to antimalarial drugs	Hypersplenism
	Lymphocyte proliferation
	Family history positive

COMPLICATIONS

- Hypersplenism (pancytopenia)
- Splenic rupture

Hypersplenism

Splenomegaly due to any cause results in sequestration and destruction of blood cells. As a compensatory mechanism, there is increased production of the cells by the bone marrow. Hypersplenism is said to be present when splenomegaly is associated with the following features:

- Anaemia
- Thrombocytopenia
- Compensatory hyperplasia in the bone marrow

Investigations

- RBC count—anaemia
- Platelets—thrombocytopenia
- Bone marrow study—marrow hyperplasia

Treatment

Hypersplenism is treated by splenectomy.

SPLENECTOMY

Indications are as follows:

S	Splenic abscess Splenomegaly (massive)
H	Hypersplenism Haemolytic anaemia—hereditary spherocytosis, autoimmune haemolytic anaemia not responding to steroids
I	Idiopathic thrombocytopenic purpura (chronic)
R	Rupture of spleen—trauma
T	Thrombosis of splenic vein—extrahepatic portal hypertension
S	Staging laparotomy in Hodgkin's disease (rarely done now) and lymphoreticular malignancies

Follow-Up

- Increased susceptibility to infections with streptococcal pneumonia and *Haemophilus influenzae*.
- In endemic areas for malaria, antimalarial chemoprophylaxis should be given.
- Erythromycin prophylaxis can be given up to 18 years of age to prevent pneumococcal infections.
- Pneumococcal vaccine should be given.

HEPATOSPLENOMEGALY

It is a condition where both the liver and the spleen are enlarged.

CAUSES

The causes of hepatosplenomegaly can be classified according to

- aetiological factors,
- presentation patterns and
- age of presentation.

Aetiological Factors

1. Infective factors
   (a) Viral
      - Hepatitis virus B, C, D—viral hepatitis, chronic active hepatitis
      - Epstein–Barr virus—infectious mononucleosis
      - Rubella
      - Cytomegalovirus

   (b) Bacterial
      - Typhoid
      - Septicaemia
      - Leptospirosis
      - Mycobacterium tuberculosis (Koch's infection)

   (c) Protozoal
      - Kala azar
      - Chronic malaria
2. Cardiac causes—congestive cardiac failure can lead to cardiac cirrhosis

3. Haematological causes—haemolytic anaemia
4. Infiltrative causes—storage disorders leading to cirrhosis
5. Malignancy—metastasis to liver
6. Metabolic causes—galactosaemia
7. Drugs—anticonvulsants

Presentation Patterns

A child with hepatosplenomegaly presents with symptoms such as fever, jaundice, anaemia, lymphadenopathy, bleeding, ascites, neurological manifestations and arthritis. According to the pattern of presentation, the causes of hepatosplenomegaly may be classified as follows:

- Hepatosplenomegaly with fever
- Hepatosplenomegaly with jaundice
- Hepatosplenomegaly with anaemia
- Hepatosplenomegaly with lymphadenopathy
- Hepatosplenomegaly with bleeding
- Hepatosplenomegaly with ascites
- Hepatosplenomegaly with neurological manifestations
- Hepatosplenomegaly with renal enlargement
- Hepatosplenomegaly with arthritis
- Hepatosplenomegaly with combination of above

Hepatosplenomegaly with Fever

1. Infections
   - Koch's infection
   - Kala azar
   - Chronic malaria
   - Acute/chronic infection
   - Infectious mononucleosis
2. Malignancy
   - Leukaemia
   - Lymphoma
3. Infiltrative—reticulosis
4. Collagen disorders
   - SLE
   - JRA

Hepatosplenomegaly with Jaundice

1. Infections
   - Viral—viral hepatitis, chronic active hepatitis, infectious mononucleosis, neonatal hepatitis
   - Bacterial—septicaemia, leptospirosis
   - Protozoal—kala azar, malaria
2. Congestive cardiac failure leading to cardiac cirrhosis
3. Haematological—haemolytic anaemia
4. Infiltrative—storage disorders leading to cirrhosis
5. Malignancy—metastasis liver
6. Metabolic—galactosaemia, cystic fibrosis, α-1-antitrypsin deficiency
7. Others—late cirrhosis, biliary atresia, choledochal cyst, drugs (anticonvulsants)

Hepatosplenomegaly with Anaemia

1. Infective causes
   - Bacterial—fulminant sepsis, infective endocarditis, disseminated tuberculosis
   - Protozoal—chronic malaria, kala azar
2. Haematological causes—haemolytic anaemia
3. Infiltrative causes
   - Reticulosis
   - Letterer–Siwe disease
4. Malignancy
   - Leukaemia
   - Lymphoma
5. Metabolic
   - Wilson's disease
   - Gaucher's disease
6. Collagen vascular disease
   - SLE
   - JRA
7. Other causes
   - Late cirrhosis with portal hypertension (hypersplenism)
   - Extreme protein energy malnutrition (PEM)
   - Osteopetrosis

Hepatosplenomegaly with Lymphadenopathy

1. Infections
   - Bacterial—mycobacterium tuberculosis (disseminated tuberculosis)
   - Viral—rubella, HIV infection, Epstein–Barr

virus (EBV) (infectious mononucleosis)
- Fungal—histoplasma (disseminated histoplasmosis)
- Protozoal—*Leishmania donovani* (kala azar)

2. Infiltrative causes
   - Reticulosis
   - Sarcoidosis
3. Malignancy
   - Leukaemia
   - Lymphoma
4. Haematological causes—thalassaemia
5. Miscellaneous causes
   - Sarcoidosis
   - Histoplasmosis
   - Pseudolymphoma syndrome

Hepatosplenomegaly with Bleeding

1. Infective
   - Bacterial—enteric fever, fulminant sepsis, infective endocarditis, leptospirosis
   - Viral—dengue
   - Protozoal—toxoplasmosis
2. Congestive—portal hypertension
3. Malignancy
   - Leukaemia
   - Lymphoma
4. Haematological
   - Chronic idiopathic thrombocytopenic purpura
   - Henoch–Schonlein purpura
5. Metabolic
   - Gaucher's disease
   - Niemann–Pick disease
6. Other causes—Reye's syndrome

Hepatosplenomegaly with Ascites

1. Infective—disseminated tuberculosis
2. Malignancy
   - Leukaemia
   - Lymphoma
   - Wilm's tumour
3. Congestive causes
   - Congestive pericarditis
   - Decompensated cirrhosis with portal hypertension
   - Congestive cardiac failure
4. Renal cause—nephrotic syndrome

Hepatosplenomegaly with Mental Retardation

- Mucopolysaccharidosis (Hurler's syndrome, Hunter's syndrome, Sanfillippo's syndrome, Sly syndrome)
- Mucolipidosis (GM1 and GM2 gangliosidosis, Wolman's disease)

Hepatosplenomegaly with seizures

1. Infective causes
   - Cerebral malaria
   - Septicaemia with meningitis
   - Neonatal hepatitis with intrauterine infection with central nervous system (CNS) manifestations
2. Storage disease
   - Infantile Gaucher's disease
   - Niemann–Pick disease type A
3. Metabolic disease
   - Galactosaemia
   - Hereditary fructose intolerance
   - Farber's disease
4. Malignancy—leukaemia with CNS secondaries
5. Other causes—hepatic encephalopathy

Hepatosplenomegaly with Arthritis/Arthralgia

1. Haematological
   - Sickle cell anaemia
   - Haemolytic anaemia with haemochromatosis
2. Collagen vascular disorders
   - SLE
   - JRA
3. Malignancy—leukaemia

Hepatosplenomegaly with Rash

1. Infections

- Viral—EBV (infectious mononucleosis, cytomegalovirus, rubella, hepatitis B)
- Bacterial—typhoid (rose spots), syphilis, brucellosis

2. Collagen vascular diseases
   - SLE (butterfly rash)
   - JRA

Hepatosplenomegaly with Malabsorption

- Cystic fibrosis
- Whipple's disease
- Wolman's disease

Hepatosplenomegaly with Renal Enlargement

- Leukaemia with renal infiltration
- Congenital hepatic fibrosis
- Zellweger syndrome
- Type I tyrosinaemia
- Widemann–Beckwith syndrome

Age of Presentation

Infancy

1. Infections
   - Intrauterine infections (TORCH infections)
   - Septicaemia
   - Neonatal hepatitis
2. Congestive causes
   - Congestive cardiac failure
   - Hepatic vein thrombosis
   - Budd–Chiari syndrome
3. Haematological
   - Haemolytic anaemia—usually seen after 6 months of age
4. Infiltrative disorders
   - Gaucher's disease
   - Glycogen storage disorders (types III, VI and IX)
   - α-1-Antitrypsin deficiency
   - Mucopolysaccharidosis
   - Haemochromatosis
5. Malignancy
   - Leukaemia (rare below 1 year of age and if it occurs, carries a bad prognosis)
   - Lymphoma
6. Metabolic
   - Wilson's disease
   - Tyrosinosis
   - Galactosaemia
7. Other causes
   - Haemangioma
   - Erythroblastosis foetalis
   - Extrahepatic biliary atresia
   - Biliary obstruction

Older Children

1. Infective causes
   - Bacterial—disseminated tuberculosis, bacterial endocarditis, liver abscess
   - Viral—infective hepatitis (acute and chronic), infectious mononucleosis
   - Fungal—histoplasmosis
   - Protozoal—malaria, kala azar
   - Parasitic—hydatid cyst (echinococcus granulosus)
2. Congestive
   - Congestive cardiac failure
   - Cirrhosis of liver with portal hypertension
   - Hepatic vein thrombosis
   - Budd–Chiari syndrome
   - Constrictive pericarditis
3. Haematological—haemolytic anaemias
4. Storage disorders
   - Gaucher's disease
   - Glycogen storage disorders
   - α-1-Antitrypsin deficiency
   - Mucopolysaccharidosis
   - Lipidosis
   - Amyloidosis
5. Malignancy
   - Leukaemia
   - Lymphoma
6. Metabolic
   - Wilson's disease
   - Cystic fibrosis
7. Nutritional—kwashiorkor (fatty infiltration)

8. Other causes
   - Haemangioma
   - Hydatid cyst
   - Malignant secondaries in the liver

CHRONIC LIVER DISEASE

Chronic liver disease refers to those conditions in which there is progressive destruction of the liver with regeneration for more than 6 months, resulting in hepatic fibrosis and cirrhosis.

CAUSES

The causes of chronic liver diseases are extensive. Following are the associated disorders:

1. Biliary causes—obstruction to the bile flow results in hepatic injury. Bile accumulates in the cytoplasm of liver cells, canaliculi and Kupffer cells, and also results in giant cell transformation of hepatocytes. The chronic liver diseases due to biliary causes include:
   - Extrahepatic biliary atresia
   - Choledochal cyst
   - Tumours obstructing the biliary tract
   - Stones in the biliary tract
   - Alagille syndrome (arteriohepatic dysplasia with intrahepatic bile duct hypoplasia)
   - Biliary hypoplasia
   - Byler's disease—progressive intrahepatic cholestasis
   - Caroli's disease—cystic dilatation of intrahepatic bile ducts predisposes to ascending cholangitis and calculus formation
   - Sclerosing cholangitis
   - Graft-versus-host disease—occurs after transplantation where antibodies formed against the graft damage the liver
   - Histiocytosis
   - Drug-induced—anabolic steroids (methyl testosterone), contraceptive steroids, erythromycin, azithromycin, ciprofloxacin, ranitidine, phenytoin, chlorpromazine, allopurinol, chlorpropamide, hydralazine, etc.
2. Hepatic causes—chronic inflammatory reaction in the liver lasting for 6 months or more can lead to chronic liver disease. The causes of chronic inflammation of liver include:
   - Infections—neonatal hepatitis; viral hepatitis B, D and C; infections such as CMV, rubella, EBV
   - Autoimmune—autoimmune chronic hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis
   - Drugs—methyl dopa, INH, ketoconazole, nitrofurantoin, amiodarone and methotrexate
   - Toxins—aflatoxin, amanita toxin and carbon tetrachloride
3. Genetic/metabolic disorders—certain genetic and metabolic disorders may also lead to chronic liver disease. The common disorders in this category include
   - α-1-Antitrypsin deficiency
   - Carbohydrate metabolism defects—galactosaemia, hereditary fructose intolerance, fructosaemia, glycogen storage disease types III and IV
   - Amino acid metabolism defects—tyrosinaemia, urea cycle disorders (carbamyl phosphate synthetase deficiency, ornithine transcarbamylase deficiency, etc.)
   - Metal storage defects—Wilson's disease, neonatal haemochromatosis
   - Lipid storage disorders—Gaucher's disease, Niemann–Pick disease type C
   - Fatty acid β-oxidation defects
   - Zellweger syndrome (cerebrohepatorenal syndrome)—absence of peroxisomes in the liver cells
   - Mitochondrial disorders (respiratory chain defects, cystic fibrosis)
4. Obstruction of hepatic veins
   - Budd–Chiari syndrome
   - Veno-occlusive disease
5. Cardiac disorders—these predispose to venous congestion in the liver. These include the following:
   - Congestive heart failure
   - Constrictive pericarditis

6. Nutritional causes
   - Hypervitaminosis A—predisposes to hepatic fibrosis or cirrhosis and veno-occlusive disease
   - Total parenteral alimentation
7. Miscellaneous
   - JRA
   - Congenital hepatic fibrosis

CLINICAL FEATURES

Onset of chronic liver diseases may be insidious or acute. Few children may be asymptomatic. Some children present with features of acute viral hepatitis. The common modes of presentation include (Box 10.7):

- Failure to thrive
- Prolonged or recurrent jaundice
- Features of portal hypertension
- Hepatomegaly or shrunken, small, hard and irregular liver
- Splenomegaly
- Ascites
- Oedema

BOX 10.7 Mnemonics for clinical presentation of chronic liver disease

A	Anorexia Alopecia Altered sensorium
B	Bowel symptoms (vomiting, constipation) Bruising (bleeding due to coagulopathy)
C	Coma Caput medusa Cruveilheir–Baumgarten sign Clay-coloured stools Clubbing
D	Delirium Disorientation Distention of abdomen (fluid or organomegaly) Dupuytren's contracture Dawson's sign (palmar erythema)
E	Ecchymosis Encephalopathy Extrapyramidal signs Oedema
F	Flapping tremor (asterixis) Foetor hepaticus Failure to thrive
G	Gastrointestinal bleed Gynaecomastia Growth failure
H	Hair loss Haematemesis Haematochezia due to rectal haemorrhoids Hepatic facies (cirrhotic facies) Handwriting change
I	Impotency in adulthood Irregular menses and amenorrhoea in adulthood Increased susceptibility to infections (spontaneous bacterial peritonitis) Infertility in adulthood (due to vitamin E deficiency) Itching due to deposition of bile salts in skin
J	Jaundice (acholuric jaundice in haemolytic jaundice)
K	Kidney failure (hepatorenal failure)
L	Lassitude Liver size (enlarged or shrunken) Loss of libido (in adulthood) Leukonychia (white nails)
M	Menarche delay Malignancy (hepatocellular carcinoma) Metabolic disorders (hypoglycaemia, hypoalbuminaemia) Muscle wasting Melaena due to portal hypertension
N	Nails (white nails due to hypoproteinaemia) Neurological signs Neurodyanamic instability Night blindness (due to vitamin A deficiency)

O	Oedema
P	Pruritus (due to bile salts deposition in skin) Pale stools (due to obstruction to bile flow) Pain in abdomen (due to distension on liver) Palmar erythema Parotid swelling Paper money skin
Q	Quiescent—due to hypoglycaemia
R	Respiratory symptoms (hepatopulmonary syndrome)
S	Steatorrhoea Secondary sexual characters loss in adulthood Spider naevi Splenomegaly Stools (clay coloured due to obstructive jaundice) Scratch marks
T	Testicular atrophy Telangiectasia
U	Ulcer (chronic leg ulcer) Urine (dark coloured)
V	Varices (oesophageal/rectal) Vitamin deficiency symptoms (for fat-soluble vitamins—A, D, E and K, as a result of fat malabsorption)
W	Wing-beating tremor
X	Xanthoma/xanthelasma

INVESTIGATIONS

Radionucleotide scans are used to establish the presence of chronic liver disease and to assess the severity of liver involvement. Other investigations are also done to find out the aetiology and complications at an early stage so that further damage to the liver can be prevented.

1. Haemogram with erythrocyte sedimentation rate (ESR)
   (a) Total count—increased in infections
   (b) Differential count—lymphocytosis in tuberculosis
   (c) ESR—elevated in infections
2. Liver function tests
   (a) Liver enzymes to test the liver cell integrity—aspartate aminotransferase (AST or SGOT), alanine aminotransferase (ALT or SGPT), serum lactate dehydrogenase (LDH-5) are elevated in liver cell injury
   (b) Investigations for biliary excretory function
      - Serum bilirubin (total, conjugated and unconjugated)—elevated
      - Serum bile acids are sensitive indicators of hepatobiliary diseases
      - Plasma membrane enzymes are increased due to damage to bile canaliculi—serum alkaline phosphatase, 5′-nucleotidase and γ-glutamyl transpeptidase (GGT)
   (c) Investigation for liver cell synthetic functions
      - Serum proteins—When the liver cells are damaged, the production of albumin is decreased. This results in reversal of the albumin–globulin ratio.
      - Prothrombin time is increased due to decreased synthesis of vitamin K-dependent factors by the failing liver.
   (d) Investigations for hepatocyte metabolism
      - Serum ammonia—increased.
      - Serum cholesterol—increased.
3. Investigations to establish liver cell injury
   (a) Liver biopsy
   (b) Tc-99 hepatic scans
4. Investigations to find out the aetiology
   (a) Markers for viral hepatitis—chronic hepatitis B (HBsAg, HBV-DNA, anti-HBe, anti-HBc IgM), chronic hepatitis C (anti-HCV, HCV-RNA), other viruses (antibodies against CMV, herpes simplex, EBV)

(b) α-1-Antitrypsin deficiency—α-1-antitrypsin levels

(c) Metabolic disorders—screening of blood and urine for metabolic disorders
- Urea cycle disorders—urine for amino-aciduria
- Wilson's disease—serum copper, hepatic copper, ceruloplasmin and 24-hour urinary copper estimation for Wilson's disease

(d) Autoimmune chronic hepatitis
- Autoantibodies (antinuclear factor [ANF], antinuclear antibodies [ANA], antismooth muscle antibodies [ASMA], liver/kidney microsomal [LKM1]) titres are more than 1:20.
- Serum IgG is increased more than 1.5 times normal.

(e) Sclerosing cholangitis
- Alkaline phosphatase—increased
- Gamma glutamyl transpeptidase—increased
- Endoscopic retrograde cholangiopancreatography (ERCP)—MRCP or operative cholangiography shows abnormalities of bile ducts such as irregular intrahepatic ducts and saccular dilatation
- Liver biopsy—may show fibrous obliterating cholangitis, periductal fibrosis, or inflammatory infiltrate, periportal copper-associated protein (Wilson's disease)

(f) Glycogen storage disorders
- Enzyme assay in the leucocytes, liver, muscle
- Liver biopsy—glycogen in the liver
- Blood sugar
- Lactate

(g) Tyrosinaemia
- Urine succinylacetone—increased
- Serum tyrosine, phenylalanine, methionine—raised

(h) Portal hypertension
- Ultrasonogram of liver
- Endoscopy

(i) Veno-occlusive disease—doppler of hepatic veins

5. Urine and stool examination
   (a) Urobilinogen in urine appears in pre-icteric phase, disappears as jaundice is evident and reappears with recovery.
   (b) Bilirubin appears in urine before clinical jaundice develops.
   (c) Stool examination may reveal steatorrhoea.
6. Investigations to find out the complications and severity of CLD
   (a) Serum electrolytes—electrolyte imbalance such as hyponatraemia
   (b) Blood glucose—decreased
   (c) Serum ammonia—elevated
   (d) Serum bilirubin—increased
   (e) Serum albumin—decreased
   (f) Prothrombin time (INR)—prolonged and unresponsive to vitamin K

TREATMENT

Treatment of chronic liver disease depends on the underlying aetiology. The aim of the treatment is to control or eliminate the underlying cause and prevent further damage to the liver. The underlying causes should be identified and treated.

1. Specific treatment should be given for conditions such as Wilson's disease, viral hepatitis and haemochromatosis. Autoimmune hepatitis can be treated with prednisolone or immunosuppressive drugs.
2. Supportive care—this includes nutrition supplementation with adequate calories and protein (Table 10.35).

TABLE 10.35 Treatment of Chronic Liver Disease

Condition	Drug	Dose
Cholestasis	Phenobarbitone	3–10 mg/kg/day
	Cholestyramine	250–500 mg/kg/day
Steatorrhoea	Formula containing medium chain triglycerides	–
Pruritis	Ursodeoxycholic acid	10–15 mg/kg/day
Vitamin deficiency	Vitamin A	10,000–25,000 unit/day
	Vitamin D (25-hydroxycholecalciferol)	3–5 µg/kg/day
	Vitamin E (1,25-dihydroxycholecalciferol)	0.05–2 µg/kg/day orally
	Vitamin K	25–200 IU/mg/day
Micronutrient deficiency	Calcium	25–100 mg/kg/day
	Phosphorous	25–50 mg/kg/day
	Zinc	1 mg/kg/day

COMPLICATIONS

Chronic liver disease may result in various complications.

H	Hepatic failure Hepatopulmonary syndrome Hepatorenal syndrome
E	Encephalopathy
P	Portal hypertension (ascites, hypersplenism, varices)
A	Ascites
T	Tumours—hepatocellular carcinoma
I	Infection—spontaneous bacterial peritonitis
C	Cirrhosis Coagulopathy—bleeding

CIRRHOSIS

Cirrhosis is a chronic, diffuse, irreversible liver damage of varied aetiology characterised by necrosis, fibrosis and widespread nodule formation due to regeneration. If left untreated, the liver loses its normal architecture and fails to carry out its normal functions. This results in complications that affect other systems of the body as well.

CAUSES

1. Infections—infections are the common cause of cirrhosis. The infections that may cause liver cirrhosis are as follows:
   - Hepatitis virus infection—the most common cause of cirrhosis is chronic infection with the hepatitis B or hepatitis C virus. Risk of the disease is greatly increased by the hepatitis D virus, which can infect only individuals who are already infected with hepatitis B. Hepatitis A and E are not associated with cirrhosis
   - CMV
   - Rubella
   - Herpes simplex
   - Coxsackie
   - Enteric cytopathic human orphan virus
   - Parasitic infections—schistosomiasis is associated with obstruction of biliary tract and cirrhosis
2. Metabolic causes—the metabolic disorders that may cause liver cirrhosis are as follows:
   - Carbohydrate metabolism—galactosaemia, glycogen storage disease type IV (Anderson disease), glycogen storage disease type III (Cori's disease), hereditary fructose intolerance
   - Protein metabolism—α-1-antitrypsin deficiency, tyrosinaemia type I, urea cycle disorders
   - Lipid metabolism—Gaucher's disease, Niemann–Pick disease type C, Wolman's disease, abetalipoproteinaemia
   - Iron—haemochromatosis
   - Copper—Wilson's disease
   - Peroxisomal disorders—Zellweger syndrome
3. Drug-induced cirrhosis—drug-induced cirrhosis may occur due to
   - Antitubercular drugs—rifampicin, INH
   - Analgesics and antipyretics—salicylates
   - Antimetabolites—methotrexate
   - Antipsychotic drugs—chlorpromazine
   - Tricyclic antidepressants—imipramine
   - Antiepileptics—diphenylhydantoin

- Antihypertensives—methyldopa
- Antiarrhythmic drugs—amiodarone
- Anaesthetic agents—halothane
- Toxins—*Amanita phalloides*, carbon tetrachloride

4. Cardiac causes—cirrhosis may occur due to the following cardiac causes:
   - Cardiac failure
   - Constrictive pericarditis
5. Vascular causes—vascular causes of cirrhosis include
   - Budd–Chiari syndrome
   - Veno-occlusive disease
6. Biliary causes—cirrhosis may occur due to the following biliary causes:
   - Extrahepatic biliary atresia
   - Intrahepatic biliary hypoplasia
   - Byler's disease
   - Alagille Watson syndrome (arteriohepatic dysplasia)
7. Autoimmune diseases—autoimmune cirrhosis occurs when the body's immune system attacks and destroys liver tissue. This may occur due to
   - SLE
   - Chronic active hepatitis
   - Primary sclerosing cholangitis
   - Primary biliary cirrhosis
8. Miscellaneous—other miscellaneous causes of cirrhosis include
   - Total parenteral nutrition
   - Cystic fibrosis
   - Cryptogenic cirrhosis
   - Budd–Chiari syndrome
   - Alcohol-induced cirrhosis (common in adults)

TYPES

Morphological Classification

Depending upon the size of the nodules, cirrhosis may be categorised into the following types:

I. Micronodular cirrhosis—The nodule size is less than or equal to 3 mm in diameter. It is seen in secondary biliary cirrhosis, haemochromatosis and alcoholic cirrhosis.
II. Macronodular cirrhosis—The nodule size is more than 3 mm in diameter. Infections of the liver usually result in macronodular cirrhosis. It is also seen in Wilson's disease and hepatitis B infection.
III. Mixed nodular cirrhosis—The nodules of varied sizes are present. It is seen in tyrosinaemia and α-1-antitrypsin deficiency.

Clinical Classification

I. Compensated cirrhosis—it refers to the early stage of progressive liver damage where there is alteration of liver architecture and abnormal liver enzymes with no abnormal physical findings on clinical examination.
II. Decompensated cirrhosis—it refers to that stage of progressive liver damage where the liver's capacity to function is compromised and a variety of complications develop throughout the body (Table 10.36).

PATHOGENESIS

Cirrhosis of liver develops insidiously as the liver damage progresses. Initially, it is well compensated with no abnormal findings on clinical examination.

TABLE 10.36 Differences between Compensated and Decompensated Cirrhosis

Features	Compensated Cirrhosis	Decompensated Cirrhosis
Liver dysfunction	Mild	Severe
Clinical features	Non-specific symptoms • Anorexia • Fatigue	Ascites Jaundice Encephalopathy Gastrointestinal bleeding
Features of liver cell failure	May be absent	Present
Liver	Firm/hard	May not be palpable
Prognosis	Good	Bad

However, the liver biopsy during this stage shows early alteration of liver architecture in the form of development of hepatic fibrosis. As the liver damage progresses, there is increased collagen deposition in the extracellular matrix and the space between the hepatocytes and sinusoids. The stellate cells which produce extracellular matrix may turn into collagen-forming cells due to a variety of paracrine factors. These factors are released by hepatocytes, Kupffer cells and sinusoidal cells following liver injury. They increase collagen deposition and lead to the capillarisation of sinusoids. Activated stellate cells also have contractile properties. Both capillarisation and constriction of sinusoids lead to the development of portal hypertension.

CLINICAL FEATURES

Compensated Cirrhosis

In the early stages, cirrhosis often does not have any overt symptoms. The few non-specific symptoms of early stage of cirrhosis are

- Easy fatigability, particularly after exercise
- Lassitude
- Itching due to a build-up of bile salts in the blood and skin
- Loss of appetite
- Low-grade fever
- Unexplained weight loss

Decompensated Cirrhosis

Decompensated cirrhosis clinically presents as a late stage cirrhosis with features of portal hypertension and hepatocellular failure in varying combinations.

Features of Liver Cell Failure

1. Jaundice due to inability of liver to conjugate the bilirubin.
2. Ascites or oedema due to retention of fluid resulting from decreased production of albumin as well as hormonal and kidney abnormalities.
3. Bleeding—decreased production of clotting factors by the liver makes cirrhotic patients prone to
   - Easy bruising
   - Haemorrhagic tendency
   - Purpura
   - Epistaxis
4. Neurological features—inefficiency of liver in breaking down toxins in the blood can affect the neurological system and cause
   - Confusion
   - Sleeplessness
   - Asterixis (flapping tremor)
   - Hepatic (portosystemic) encephalopathy
   - Coma
5. Cachexia—liver enzyme derangement can result in a general loss of weight and strength due to poor absorption of nutrients.
6. Liver size—hepatomegaly in earlier stages and shrinkage of liver in later stages.
7. Circulatory changes
   - High volume pulse
   - Flushed face due to hyperdynamic state
   - Spider naevi (dilated central arteriole with radiating vessels are seen in the areas which are drained by SVC such as face and upper part of the chest. If the number is more than five, it is significant. It is due to high oestrogen levels in the blood
   - Palmar erythema—hands are warm and red (Dawson's sign)
   - Cyanosis
8. Endocrine changes occur due to excess of hormones such as oestrogen which are not metabolised by the failing liver.
   - Hair loss—alopecia, loss of axillary and pubic hair
   - Men—gynaecomastia, testicular atrophy, impotence, loss of libido (seen in adolescents and adults)
   - Women—breast atrophy, irregular menses, amenorrhea (seen in adolescents and adults)
9. Fetor hepaticus—due to mercaptans (methionine converted into methyl mercaptans)
10. Skin changes
    - Paper money skin—also known as American dollar sign.

- Pigmentary changes—white spots may be seen on the arms and buttocks. Diffuse pigmentation may be seen.

11. Fingers—clubbing
12. Nail changes
    - Leukonychia—white nail due to hypoalbuminaemia.
    - Terry nails—80% of the nail in the proximal part are opaque with characteristic ground glass appearance and the remaining 20% are pink. This is seen in fingers and toes. This is best seen in the thumb and index fingers. This is due to decrease in vascularity and increase in connective tissue in the nail bed.

Features of Portal Hypertension

- Splenomegaly
- Collateral vessels between systemic and portal systems such as caput medusae
- Variceal bleeding

COMPLICATIONS

If cirrhosis is not treated at an early stage, it leads to complications which may result in death of the patient.

1. Hepatic encephalopathy
2. Hepatopulmonary syndrome
3. Bleeding manifestations
    - Variceal bleeding
    - Bleeding due to congestive gastropathy
    - Hepatic coagulopathy
4. Hepatorenal syndrome
5. Metabolic causes such as hypoglycaemia
6. Electrolyte imbalance (hypokalaemia, hyponatraemia)

INVESTIGATIONS

Investigations are done to find out the aetiological factors and to assess the extent of liver damage.

1. Liver function tests
    - Serum proteins—total serum proteins and serum albumin are decreased. Gamma globulin levels are increased. A:G ratio is reversed.
    - Prothrombin time—increased (normal PT is 12–16 seconds).
    - Serum bilirubin—elevated.
    - Serum cholesterol is low.
    - Liver enzymes—elevated AST (SGOT), ALT (SGPT), serum alkaline phosphatase, 5′-nucleotidase and GGT.
2. Thymol turbidity test is positive in hyperglobulinaemia.
3. Urine for urobilinogen is positive.
4. Endoscopic examination of the upper GIT is done to show the site and extent of varices.
5. Imaging studies
    - Barium swallow to reveal varices.
    - Ultrasound findings—heterogeneous echo pattern, decreased liver size, distortion in architecture, with regenerating nodules. Other findings that may be seen are increased portal vein size, splenic enlargement and free fluid in abdomen.
    - CT scan—normal attenuation in the areas of fibrosis and degeneration, decreased attenuation in the areas of fatty infiltration, small liver with irregular nodules and collateral vessels.
    - MRI scan—it shows the anatomic abnormalities. The regenerating nodules may show reduced signal intensity due to iron deposition.
6. Liver biopsy to confirm the diagnosis of cirrhosis. The surest way to diagnose cirrhosis, especially in the earlier stages when symptoms are minimal, is by liver biopsy.
7. Investigations to find out the aetiology
    - Complete haemogram to detect infection
    - Viral serology for hepatitis B virus
    - TORCH screening
    - Urine and blood screening for metabolic disorders (galactosaemia, tyrosinaemia, glycogen storage disorders)
    - Serum copper, ceruloplasmin and liver biopsy to detect Wilson's disease
    - Sweat chloride test to detect cystic fibrosis
    - α-1-Antitrypsin deficiency
    - Serum ferritin level, iron levels and iron

binding capacity to detect haemochromatosis
- Liver biopsy for liver tissue copper content estimation (increased in Wilson's disease)

TREATMENT

Treatment is aimed to provide support to the liver so that the liver can regenerate. The substances which are metabolised or detoxified in the liver should be withheld. The causative factors should be treated.

Supportive Treatment

- Bed rest.
- Diet modification—avoid high protein diet. Protein restriction in the diet is not indicated in Grade I and II encephalopathy. Vegetable proteins should be preferred. In fats, medium chain triglycerides (MCT) should be given as they do not require liver for metabolism.

Treatment of Infections

Infections that cause cirrhosis should be treated with drugs, depending on the causative factors (bacterial or viral).

- Broad spectrum antibiotics prevent bacterial infections which may predispose to hepatic encephalopathy.
- Spontaneous bacterial peritonitis may be treated with amoxicillin or cefotaxime.
- Liver damage due to hepatitis B or C virus can be limited by antiviral agents such as interferon.

Specific Treatment

Cirrhosis is irreversible, but treating the underlying cause of the liver damage can dramatically limit further destruction of liver tissue and help prevent the development of complications. In patients with haemochromatosis, removal of blood (phlebotomy) to decrease iron levels in the body helps prevent liver damage. Table 10.37 summarises the specific treatment done in various conditions that lead to cirrhosis.

TABLE 10.37 Treatment of Conditions Leading to Cirrhosis

Conditions	Treatment
Wilson's disease	D-Penicillamine trientine dihydrochloride
Autoimmune hepatitis	Corticosteroids Azathioprine
Haemochromatosis	Desferrioxamine Phlebotomy
Coagulopathy	Injection vitamin K

Treatment of Complications

In advanced cases of cirrhosis, the goal of treatment is management of complications such as fluid retention, internal bleeding and neurological symptoms. When drugs and other medical interventions can no longer control such complications, liver transplantation can be lifesaving.

PROGNOSIS

Prediction of prognosis is based on various criteria and scoring systems such as the Child–Pugh scoring and Model for End-Stage Liver Disease (MELD) scoring. A few salient factors, on which the prognosis of cirrhosis depends, are given in Table 10.38.

Child–Pugh Scoring

Child–Pugh scoring is used to evaluate the prognosis in cirrhosis and is based on the presence of hepatic encephalopathy, ascites, level of serum bilirubin, serum albumin and prothrombin time (Table 10.39). The total score is added to classify the disease into Child–Pugh class A (5–6 points), B (7–9 points) or C (10–15 points). Class A has the best prognosis in terms of highest survival rate and least perioperative mortality.

MELD Scoring

Model for End-Stage Liver Disease (MELD) scoring is also used for assessing the patients for liver transplantation and postoperative survival rate. It is based on the levels of serum bilirubin, INR, serum creatinine and aetiological factors resulting in cirrhosis (1 for alcohol and 2 for other causes).

TABLE 10.38 Assessment of Prognosis in Cirrhosis

Factors	Good Prognosis	Bad Prognosis
Age	Young age	Advanced age
Nutritional status	Good nutrition	Poor nutrition
Aetiological factors	Hepatitis B Wilson's disease Alcohol induced	Hepatitis C, D
Morphological factors	Macronodular/ micronodular with regenerating nodules	Distortion of architecture of liver cells
Evolution	Progression slow Regressing	Rapidly shrinking liver size
Clinical features	Large liver	Marked ascites Gastrointestinal tract bleeding Spontaneous bleeding from other sites Persistent hypotension (systolic pressure <100 mm Hg)
Investigations	Fatty liver Normal liver functions	Low prothrombin level—persistent High serum bilirubin High alkaline phosphatase Low albumin <2.5 g/dL
Response to therapy	Present	Absent
Complications	Extensive collaterals	Progressive neurological complications Variceal bleeding with liver cell failure Portal hypertension with bleeding manifestations Hepatocellular failure

The score is used to assess the prognosis at 7 days, 30 days and 90 days in the postoperative period. High scores are associated with higher mortality. Calculation of MELD score is done by using the following formula:

$$\text{MELD} = 3.8\,[\ln \text{bilirubin (mg/dL)}] + 11.2\,(\ln \text{INR}) + 9.6\,[\ln \text{creatinine (mg/dL)}] + 6.4\,(\text{aetiology})$$

ln is logarithm.

PREVENTION

It consists of the following measures:

- Vaccination against hepatitis B in high-risk group children
- Early diagnosis and treatment of hepatitis B and C
- Use of disposable needles for injections
- Proper screening of blood before transfusion
- Early diagnosis and treatment of haemochromatosis by venesection, Wilson's disease with chelating agents
- Avoiding exposure to toxic agents
- Abstinence from alcohol and safe sex practices in adults and adolescents

PORTAL HYPERTENSION

Portal hypertension refers to an increased pressure gradient in the portal venous system. The normal portal pressure is 7–10 mm Hg or 10–15 cm saline. In portal hypertension, the portal pressure increases to more than 12 mm Hg or 30 cm saline. Also, the intrasplenic pressure is more than 17 mm Hg or wedge hepatic pressure is 4 mm Hg or more above the IVC pressure.

TABLE 10.39 Child–Pugh Scoring

Parameters	1	2	3
Hepatic encephalopathy (stage)	None	1 and 2 stages (or suppressed with medications)	3 and 4 stages (or refractory)
Ascites	Absent	Mild—controlled medically	Moderate—poorly controlled
Total serum bilirubin (mg/dL)	<2	2–3	>3
Serum albumin (g/dL)	>3.5	2.8–3.5	<2.8
Prothrombin time (prolonged in seconds) or Prothrombin time INR	<4 seconds or <1.7	4–6 seconds or 1.7–2.2	> 6 seconds or >2.2

ANATOMY OF PORTAL SYSTEM

The venous blood from major part of GIT drains to the liver by the portal venous system. The portal system begins as a capillary plexus in the mesentery of the intestine and ends in the sinusoids of the liver. Portal vein is an important component of the portal system. It drains blood from the spleen, pancreas, gallbladder and the digestive tract from the lower third of the oesophagus (except the lower part of rectum and anal canal) to the liver. Superior mesenteric vein and splenic vein anastomose to form the portal vein at the level of L_2 vertebra, posterior to the neck of pancreas. Tributaries of the portal vein are as follows (Fig. 10.19):

- Superior mesenteric vein—it receives the jejunal, ileal, middle colic, ileocolic, right colic, right gastroepiploic and inferior pancreatico duodenal veins
- Splenic vein—it receives the inferior mesenteric (continuation of superior rectal vein and receives the sigmoid and left colic veins), left gastroepiploic, short gastric and pancreatic veins (Fig. 10.20)
- Left gastric vein (coronary vein)
- Right gastric vein
- Cystic veins
- Paraumbilical veins
- Superior pancreaticoduodenal veins

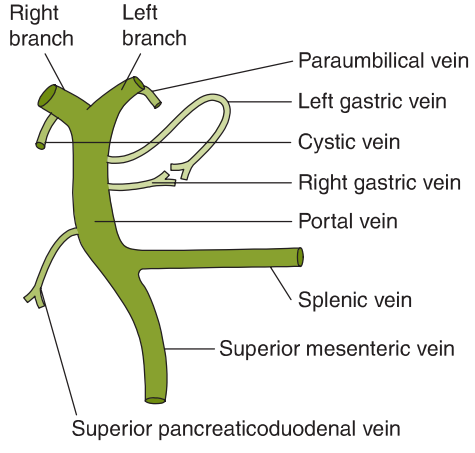


FIGURE 10.19 Tributaries of portal vein.

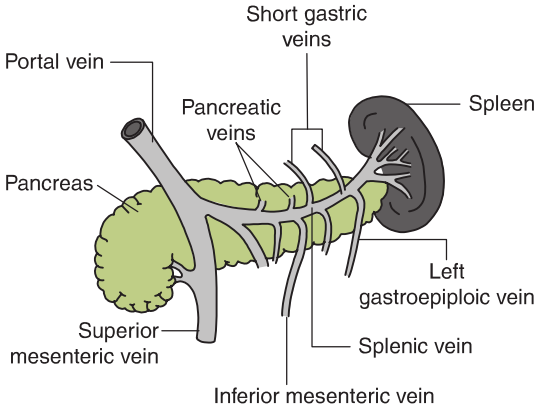


FIGURE 10.20 Tributaries of splenic vein.

MEASUREMENT OF PORTAL VENOUS PRESSURE

Portal venous pressure can be measured through the spleen, liver or portal vein. It is not done routinely as it is very invasive. It is done only for research purposes. Portal hypertension is gauged more by its clinical features. It is measured by

- Percutaneous intrasplenic measurement of portal pressure
- Catheterisation of hepatic vein

Table 10.40 gives a comparative depiction of the normal pressure versus pressure in portal hypertension at various sites of measurement.

TABLE 10.40 Normal Pressure versus Pressure in Portal Hypertension

Features	Normal (mm Hg)	Portal Hypertension (mm Hg)
Portal venous pressure	7–10	>12
Intrasplenic pressure	<17	>17
Wedge hepatic pressure	<6	>6

CLASSIFICATION

Portal hypertension occurs due to obstruction in the portal vessels. It is classified as follows on the basis of site of increased resistance in the portal system (Table 10.41).

I. Prehepatic
II. Intrahepatic
III. Posthepatic

TABLE 10.41 Classification of Portal Hypertension

Portal Hypertension	Causes
Prehepatic (obstruction before the veins reach the liver)	Idiopathic Developmental defects Portal vein thrombosis due to sepsis (umbilical, portal pyaemia) or procoagulopathy (protein C or S, antithrombin III deficiency) Abdominal trauma Postoperative Malignant disease of pancreas or liver Pancreatitis causing isolated splenic vein obstruction Portal lymphadenopathy in lymphoma—hyperviscosity syndromes Intraluminal trauma of portal vein due to catheterisation Injury to the biliary tract near the porta hepatis due to the trauma or surgery
Intrahepatic (obstruction in the liver)	Infections—cirrhosis due to hepatitis B, C Metabolic disorders—Wilson's disease Cholestatic disorders—biliary atresia, neonatal hepatitis Congenital hepatic fibrosis Chronic active hepatitis Chronic myeloid leukaemia Lymphoma Sarcoidosis Leukaemic infiltrations Primary biliary cirrhosis Schistosomiasis Wilson's disease α-1-Antitrypsin deficiency Glycogen storage disease type IV Drugs—methotrexate, 6-mercaptopurine, azathioprine Toxins—arsenic, vinyl chloride, hypervitaminosis A Idiopathic Parenteral nutrition
Posthepatic (obstruction of flow from liver to IVC or to the right side of heart)	Budd–Chiari syndrome Constrictive pericarditis Veno-occlusive disease

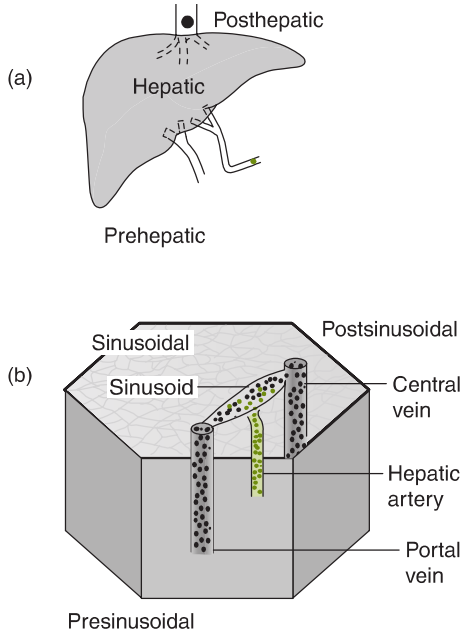


FIGURE 10.21 Types of portal hypertension.

Differences between prehepatic and intrahepatic portal hypertension are given in Table 10.42.

It can also be classified as presinusoidal, sinusoidal and postsinusoidal on the basis of increased resistance in relation to sinusoids present in the liver (Figs. 10.21 and 10.22).

PORTOSYSTEMIC COLLATERALS

The increased pressure in the portal system leads to development of shunts from portal system to systemic system. This helps in decompressing the portal venous system (Fig. 10.23).

Existing Tributaries

Normally, some portosystemic collaterals are present but the blood flow in these becomes significant only in the presence of portal hypertension. These are given in Table 10.43. There is dilatation and reversal of blood flow in the already existing tributaries.

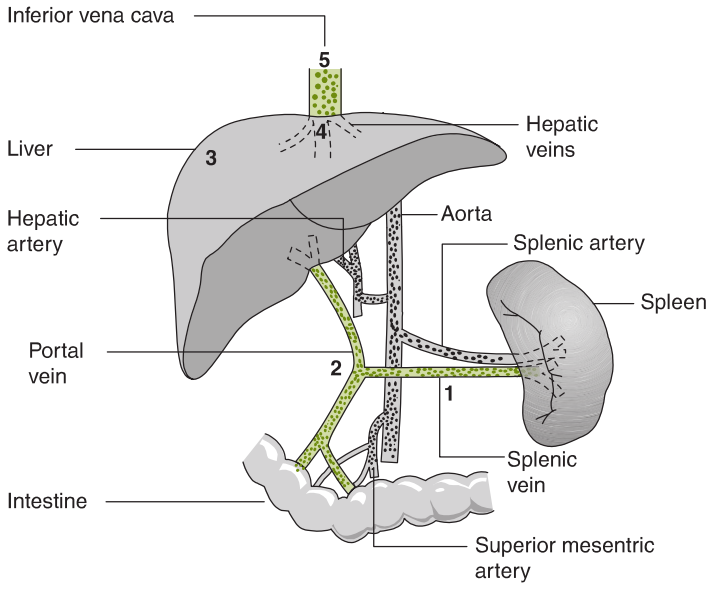


FIGURE 10.22 Sites of obstruction in portal hypertension. 1, splenic vein; 2, portal vein; 3, liver; 4, hepatic vein; 5, IVC.

TABLE 10.42 Differences between Prehepatic and Intrahepatic Portal Hypertension

Features	Prehepatic	Intrahepatic
Site	Obstruction before the veins reach the liver	Obstruction in the liver
Causes	Developmental defects Umbilical sepsis—thrombus Trauma—umbilical cord cauterisation Intra-abdominal sepsis Postoperative Idiopathic	Congenital hepatic fibrosis Chronic active hepatitis
Clinical features	Upper GI bleed splenomegaly	Upper GI bleed Hepatomegaly Splenomegaly Ascites
Dilated anterior abdominal veins	Absent	Present
Liver	Normal	Cirrhosis
Hepatomegaly	Rare	Can be present
Complications	Upper gastrointestinal bleeding	Hepatic encephalopathy
Treatment	Bleeding control from varices	treatment of the cause Liver transplantation

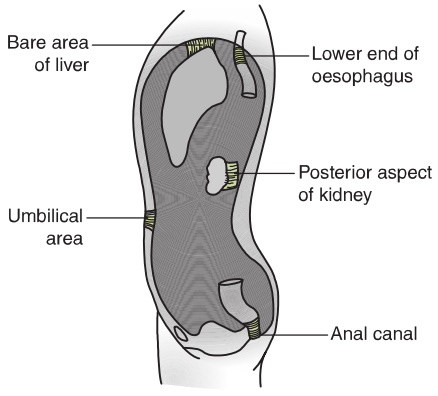


FIGURE 10.23 Sites of portosystemic anastomoses.

New Collaterals

Apart from the existing collaterals, new collateral will form as a result of portal hypertension. Development of new collaterals is seen in conditions causing intrahepatic portal hypertension such as cirrhosis. Table 10.44 gives the various sites of new portosystemic collaterals and their clinical presentation.

TABLE 10.43 Sites of Portosystemic Collaterals—Existing Tributaries

S. No.	Site of Porta-Systemic Collaterals	Portal Vessels	Systemic Vessels	Clinical Presentation
1	Gastro-oesophageal junction—plexus around the lower end of oesophagus	Oesophageal tributaries of left gastric vein and short gastric vein	Intercostal veins, oesophageal and azygous, diaphragmatic veins, accessory haemiazygos vein	Oesophageal varices (submucosal venous plexuses in the oesophagus and stomach) Haemetemesis Malena
2	Anorectal junction—plexus around the lower third of rectum and anal canal	Superior rectal vein (which drains to inferior mesenteric vein which drains to splenic vein)	Middle and inferior rectal vein (middle rectal vein drains to internal iliac vein and inferior rectal vein drains to internal pudental vein)	Rectal varices haemorrhoids
3	Mesenteric venous plexus	Superior mesenteric vein	Mesenteric venous plexus which joins IVC through retroperitoneal veins	Silent (congestion of mesenteric venous plexus)

TABLE 10.44 Sites of New Portosystemic Collaterals

S. No.	Sites of New Portosystemic Collaterals	Portal Vessels	Systemic Vessels	Clinical Presentation
1	Anterior abdominal wall—around the umbilicus	Postumbilical vein supplied by recanalised umbilical vein (along the round ligament of liver)	Superficial veins of anterior abdominal wall (superficial branches of superior epigastric vein drain into SVC, superficial epigastric and circumflex iliac vein drain into IVC)	Caput medusae
2	Posterior abdominal wall Retroperitoneal tissue, extraperitoneal surface of the abdominal organs wherever the organs are in contact with the retroperitoneal tissue or abdominal wall (gastrorenal, splenoperitoneal)	Portal vein branches	Veins of posterior abdominal wall	Silent
		Veins of retroperitoneal organs such as duodenum, descending colon	Subdiaphragmatic veins and retroperitoneal veins	
		Tributaries of the superior and middle mesenteric vein of portal vein	Veins of the abdominal wall and veins of renal capsule	
		Splenic vein	Renal and azygos vein	
3	Bare area of liver	Veins of Sappey, Omental veins	Subdiaphragmatic veins—veins over the bare area of liver	Silent
4	Splenorenal collaterals	Left renal vein	Splenic or diaphragmatic, pancreatic, left adrenal vein	Silent
5	Gastrorenal collaterals	Gastric vessels	Renal vessels	Silent
6	Splenoperitoneal collaterals	Splenic vessels	Peritoneal vessels	Silent
7	Liver	Left branch of portal vein	IVC	Patent ductus venosus

Bridging Collaterals

These are seen in prehepatic portal hypertension. These collaterals maintain a normal hepatic blood flow. Hence, the direction of flow is towards the liver.

CLINICAL FEATURES

Children with portal hypertension usually present with ascites, bleeding from gastro-oesophageal varices, splenomegaly and caput medusa.

Symptoms

The symptoms of portal hypertension include

- Haematemesis due to bleeding from oesophageal varices (portosystemic shunts)
- Haematochezia—bleeding of frank blood from rectum due to bleeding from rectal varices
- Melaena due to bleeding in the gut
- Ascites
- Altered sensorium/encephalopathy due to portosystemic shunting which results in toxic substances reaching the brain

Signs

The signs of portal hypertension include the following:

- Ascites
- Bleeding from oesophageal varices—acute/chronic
- Caput medusae collaterals (portosystemic shunts)
- Cruveilhier–Baumgarten syndrome—continuous murmur heard over the umbilical area due to increased flow in the umbilical veins
- Splenomegaly—can be symptomless/present with features of hypersplenism
- Signs of liver cirrhosis or liver cell failure such as jaundice and spider naevi
- Hepatomegaly
- Signs of hepatic vein thrombosis—absent hepatojugular reflex, tender hepatomegaly and splenomegaly

INVESTIGATIONS

The investigations advised in cases with portal hypertension include

1. Complete haemogram—to detect infection
2. Liver function tests—to detect hepatocellular failure
3. Endoscopy of the upper GIT—to reveal evidence of varices, congestive gastropathy and gastric varices. Duodenal varices may be seen. In superior mesenteric vein obstruction isolated duodenal varices may be seen
4. Barium swallows—to detect varices. Oesophageal varices may be found in barium meal examination; it appears like a bag of worms best seen in the lateral anterior oblique view. The appearance becomes prominent when the child performs Valsalva manoeuvre. Double contrast studies show gastric varices
5. Ultrasonogram
   - Increased echogenicity in cirrhosis and ascites
   - To detect increased portal vein size
   - Free fluid in the abdomen and splenic enlargement
   - Ratio of diameter of the portal vein (in millimetres) to the body surface area (in square metres) >12 in portal hypertension
   - Vascular collaterals in the omentum which are thickened
   - Cystic dilatations of intrahepatic bile ducts in congenital hepatic fibrosis
   - Abnormal hepatic veins in Budd–Chiari syndrome
6. Doppler studies (to detect portal vein dilatation and direction of portal flow)—in normal children, the diameter of the portal vein increases during inspiration but is absent in portal hypertension. Direction of flow in the portal vein is reversed in severe portal hypertension
7. Portal angiogram
8. Digital subtraction angiography
9. CT scan
10. MRI scan
11. Percutaneous intrasplenic measurement of portal pressure
12. Measurement of wedge hepatic venous pressure is helpful to determine the site of obstruction in relation to the sinusoids. It is measured by passing a catheter through the SVC or IVC into the hepatic veins and then to the hepatic venous radicle. It is normal in extrahepatic and intrahepatic presinusoidal but increased in intrahepatic sinusoidal and intrahepatic postsinusoidal portal hypertension
13. Venography to find out the site of obstruction
    - Percutaneous transhepatic catheterisation for venography
    - Splenoportovenography

TREATMENT

The causative factors should be identified and treated. Other measures are discussed next.

Supportive

- If the child is in shock, the child would have lost about 40% of the blood volume or more. The hypovolaemia should be corrected by intravenous infusion of fluids such as normal saline, ringer lactate or blood. The central venous pressure should be monitored along with vital signs and urinary output.
- Oxygen saturation should be maintained by administration of oxygen by nasal canula or mask.
- Nasogastric aspiration helps remove the blood from the stomach.

Medical

- Beta-blockers—propranolol in the dose of 1 mg/kg/day. Propranolol reduces both systemic and portal pressures by its vasodilatory actions. It also decreases the cardiac output, thereby reducing the blood pressure.
- Haematemesis—treatments to stop oesophageal variceal bleeding and to prevent recurrent bleeding (refer section *Variceal Bleeding*).
- Treatment of causative factors.

Surgical

The indications for surgery in portal hypertension include

- Recurrent variceal bleeds
- Hypersplenism
- Portal hypertension due to extrahepatic or intrahepatic presinusoidal type

Surgical treatment involves creation of portacaval shunts to decompress the portal system.

- Distal splenorenal shunt
- Sugiura operation is gastro-oesophageal devascularisation for oesophageal varices. The oesophageal and gastric venous plexus are divided from the portal collateral vessels. The extra-oesophageal systemic venous collaterals involving the azygous system are preserved. Splenectomy can be done at the same time.
- Modified Sugiura procedure—transjugular intrahepatic portosystemic shunt (TIPS)

COMPLICATIONS

- Hypersplenism with sequestration of RBCs, white blood cell (WBC) and platelets causing pancytopenia
- Ascites
- Hepatorenal syndrome
- Hepatic encephalopathy
- Variceal bleeding (GI bleeding from oesophageal/gastric varices or from congestive gastropathy)
- Increased risk of spontaneous bacterial peritonitis

PROGNOSIS

The unfavourable prognostic signs of portal hypertension include

- Jaundice
- Ascites
- Hypoalbuminaemia
- Encephalopathy

VARIANTS

Sinistral Portal Hypertension

Left-sided portal hypertension is due to obstruction of the splenic vein. Predisposing cause is pancreatitis. This is known as sinistral portal hypertension.

Hyperkinetic Portal Hypertension

Both intrahepatic and extrahepatic arteriovenous fistulae cause this type of portal hypertension. Predisposing conditions include trauma, Osler–Rendu–Weber syndrome and hypersplenism. It is detected by arteriography.

VARICEAL BLEEDING

Variceal bleeding is gastrointestinal bleeding from

oesophageal/gastric varices or from congestive gastropathy. The common sites of varices are

- Gastro-oesophageal junction at the cardia
- Rectal varices
- Gastric varices
- Duodenal varices

CAUSES OF VARICES

- Portal hypertension due to cirrhosis and chronic hepatitis
- Splenic vein thrombosis (results in oesophageal varices without increased portal venous pressure)

PREDICTORS OF BLEEDING

- Size of the varices—the larger the size, the more likely it is to bleed
- Red signs (e.g., red whale markings, cherry red spots)—presence of red colour correlates with the flow of blood through the varices
- Hepatocellular function—hepatic failure promotes bleeding
- Hepatic venous pressure gradient >12 mm Hg

PREDISPOSING FACTORS

- Increased intra-abdominal pressure during lifting weight, straining
- Site—longitudinal tortuous veins at the lower end of oesophagus are susceptible to haemorrhage
- Infections

CLINICAL FEATURES OF VARICES

The child is asymptomatic until the varices start bleeding. The child presents with the following symptoms:

- Haematemesis (congestive gastropathy)
- Melaena
- Haematochezia

INVESTIGATIONS

- Blood counts—to rule out infections
- Haematocrit—decreased in severe bleeding
- Prothrombin time
- Blood grouping and cross matching
- Barium swallows show filling defects in the lower end of the oesophagus
- Endoscopy—varices can be visualised and assessed for the risk of bleeding by oesophagoscopy. High risk is associated with large varices, red signs (e.g., red whale markings, cherry red spots) and hepatic venous pressure gradient >12 mm Hg
- Invasive procedures—splenoportography (by injecting radio-opaque dyes in the splenic pulps), superior mesenteric angiography (by injecting radio-opaque dyes into the superior mesenteric artery)
- Investigations for predisposing factors—liver function tests (high bilirubin and low albumin)

ENDOSCOPIC GRADING

This is important as there is a direct relation between the risk of bleeding and the size of the varices, as assessed by endoscopic examination (Fig. 10.24). Two different methods of grading are given in Tables 10.45 and 10.46.

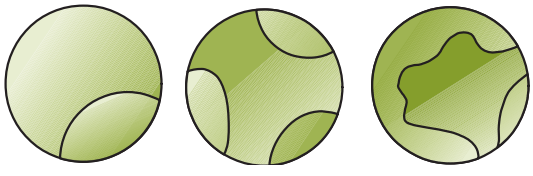


FIGURE 10.24 Grading of varices by endoscopic examination. (a) Grade I. (b) Grade II. (c) Grade III.

TABLE 10.45 Grading of Varices

Grade	Endoscopic Findings
1	Varices visible but can be compressed by the endoscope
2	Varices visible but cannot be compressed by the endoscope
3	Varices are confluent around the circumference of the oesophagus

TABLE 10.46 Alternative Method of Grading of Varices

Grade	Endoscopic Findings
I	Not visible during routine examination. The varices are visible on inspiration only, single in number, but can be compressed and obliterated.
II	Visible during routine examination. The varices are seen in both inspiration and expiration, compressible.
III	Varices are projecting into oesophageal lumen, less than 50%, not compressible, red or blue.
IV	The varices may project into oesophageal lumen, more than 50% or completely.

TREATMENT

Variceal bleeding is an emergency and should be managed in an intensive care setting. Treatment should be safe, effective and easy to administer. The aim of the treatment is to control or stop the bleeding and to reduce the portal venous pressure. Treatment in a child with GI haemorrhage includes the following:

- Measures to control or stop the bleeding—this includes pharmacotherapy, balloon tamponade, endoscopic sclerotherapy, endoscopic band ligation, TIPS, etc.
- Pharmacologic reduction of portal venous pressure
- Surgical treatment—this includes devascularisation procedures, shunt surgeries and liver transplant
- Therapeutic radiological interventions
- Supportive care—antibiotics, correction of coagulation disorders and maintenance of normal plasma volume
- Treatment of the primary cause

Measures to Control or Stop the Bleeding

In most of the children, haematemesis stops spontaneously with blood transfusion. Other modalities include pharmacotherapy, balloon tamponade, endoscopic sclerotherapy, endoscopic band ligation and TIPS. Some of these are described as follows:

1. Balloon tamponade—this is a temporary procedure which is done if oesophageal variceal bleeding persists despite adequate medical treatment and blood transfusion. The tubes used for balloon tamponade are Minnesota tube, Sengstaken–Blackmore tube and Linton–Nachalas tube. The tube should be tested under water for leakage and the position be checked radiologically. This procedure should always be done in a hospital setup.
2. Endoscopy—this is done to establish the cause of bleeding and to control the bleeding. Therapeutic endoscopy is the mainstay of treatment in emergency conditions and has replaced balloon tamponade which was more dangerous. Two types of interventions are done in therapeutic endoscopy, endoscopic sclerotherapy and variceal ligation or banding.
   (a) Endoscopic sclerotherapy—controls bleeding in up to 90% of patients. The sclerosants that can be used are polidocanol, ethanolamine oleate, sodium tetradecyl sulphate and sodium morrhuate. Injection can be repeated until the varices are obliterated. The complications include mucosal ulceration, bleeding, oesophageal perforation, mediastinitis and pulmonary complications. Long-term complications may be oesophageal stricture and rebleeding (45% cases).
   (b) Variceal ligation or banding—it is indicated if the haemorrhage is not controlled within two sessions of sclerotherapy. In this procedure, a banding device is attached to the tip of the endoscope. One to three bands are used for each varix. Banding results in strangulation, sloughing and fibrosis. Rebleeding occurs in 26% of the cases. Local complications are less common in this method than sclerotherapy. Table 10.47 summarises the salient features of these two procedures.

Pharmacologic Reduction of Portal Venous Pressure

This can be achieved either by reduction of splanchnic blood flow or by decrease in intrahepatic resistance.

TABLE 10.47 Salient Features of Endoscopic Sclerotherapy and Variceal Ligation

Features	Endoscopic Sclerotherapy	Endoscopic Variceal Ligation
Material used	Sclerosants	Bands
Mechanism	Chemical	Physical obstruction
Effectiveness	Controls bleeding in up to 90% cases	Controls bleeding in >90% cases
Rebleeding	45%	26%
Local complications	More common	Less common
Oesophageal strictures	More common	Less common

Drugs used for reduction of splanchnic blood flow are β-blockers, vasopressin/terlipressin and somatostatin/octreotide. Drugs used for decreasing intrahepatic resistance are nitroglycerine, isosorbide dinitrate and isosorbide mononitrate. These are described as follows:

1. Non-selective β-blockers—propranolol, nadolol and timolol can be used. These decrease the variceal bleeding by 45%. The dose of propranolol is 0.5–1 mg/kg/day orally every 6–8 hourly. In some children, 2–4 mg/kg/day may be needed. Nadolol has a long half-life and can be used in single daily dose. A fall in pulse rate by 25% below the baseline is useful to monitor the efficacy of β-blockers. If there is failure to respond to β-blockers, second drug nitroglycerine can be added. Beta-blockers are contraindicated in bronchial asthma, chronic obstructive lung disease and insulin-dependent diabetes mellitus. Long-acting nitrates such as isosorbide-5-mononitrate can be used when β-blockers are contraindicated.
2. Vasoconstrictors
   - Vasopressin (Pitressin)—it results in vasoconstriction due to smooth muscle constriction in the splanchnic, portal and intrahepatic vessels. It reduces the portal pressure without decreasing the systemic pressure. Coronary vasoconstriction can be avoided by giving it along with nitrates. Dose used in children is 0.002–0.005 U/kg/minute intravenously and should not exceed 0.01 U/kg/minute. This is given for 12 hours and tapered over next 24–48 hours.
   - Terlipressin (Glypressin)—it is a synthetic analogue of vasopressin given as 2 mg bolus every 4 hours intravenously till the bleeding stops and followed by 1 mg until the child is not bleeding for 24–48 hours.
3. Antisecretory agents
   - Somatostatin—it is a splanchnic vasoconstrictor used for reduction of portal venous pressure. It decreases blood flow in the portal system due to vasoconstriction. It is rapidly cleared from circulation and does not cause coronary vasoconstriction. Dose used is 1–2 μg/kg bolus up to a maximum of 50 μg followed by a constant infusion of 0.4–2 μg/kg for 5 days.
   - Octreotide—it is a synthetic somatostatin analogue similar in action but is more potent and has longer duration of action. Dose used is 1–2 μg/kg bolus followed by 1 μg/kg/hour every 8–12 hourly. It can be given up to 1–10 μg/kg every 12 hourly diluted in 50–100 mL normal saline or 5% dextrose.
4. Vasodilators—they decrease the intrahepatic vascular resistance without decreasing peripheral or portal collateral resistance.
   - Nitroglycerine—it stimulates cyclic guanosine monophosphate (cGMP) production resulting in vascular smooth muscle relaxation and decrease in blood pressure. Nitroglycerine 0.25–0.50 μg/kg/minute, given intravenously for 12–24 hours along with vasopressin, lowers the portal pressure. This counteracts the side effects of vasopressin.
   - Other vasodilator drugs used are isosorbide mononitrate, isosorbide dinitrate, nitrates and verapamil.

Surgical Management

If the bleeding is not controlled by medical treatment, consider control of bleeding by surgical means.

Indications

- Non-compliance or failure to endoscopic sclerotherapy

- Recurrent bleeds after four to six sessions of endoscopic sclerotherapy
- Ectopic varices
- Hypersplenism

Types

1. Decompressive shunts
   - Portacaval shunts—side-to-side anastomosis of the portal vein to the IVC so that the portal vein is decompressed into the vena cava.
   - Selective shunts—splenorenal or mesocaval shunts.
   - Splenorenal anastomosis is done in children with portal vein thrombosis. It is contraindicated if the splenic artery <1 cm in diameter.
   - Partial shunts—interposition of portacaval/mesocaval polytetrafluoroethylene grafts.
2. Non-decompressive surgery
   - Oesophageal transection—resection and reanastomosis of the lower end of oesophagus.
   - Oesophageal devascularisation (Sugiura procedure with splenectomy and Hassab modification without splenectomy)—devascularisation is done by staple gun transection of lower oesophagus.
   - Splenectomy for treatment of oesophageal varices due to splenic vein thrombosis.
3. Orthotopic liver transplantation in advanced liver disease

Therapeutic Radiological Interventions

Indications

- Haemorrhage not controlled by medical and endoscopic modalities
- Contraindications for surgical intervention

Procedures

- Percutaneous transhepatic embolisation (PTE) is less effective than medical and surgical modalities.
- Transjugular intrahepatic portosystemic shunt—an expandable metallic stent is placed between the hepatic and portal veins in the liver

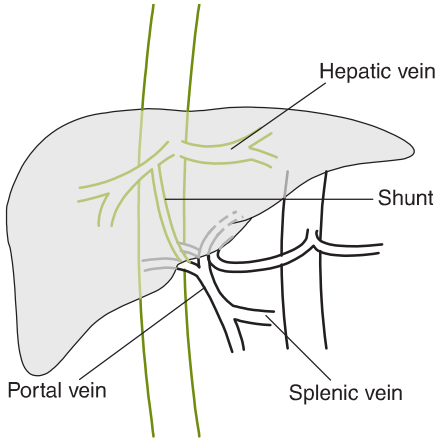


FIGURE 10.25 Transjugular intrahepatic portosystemic shunt.

(Fig. 10.25). The stent is inserted through the jugular vein and right hepatic veins under radiological guidance. The procedure is less invasive than surgical shunts. It is indicated if the variceal bleeding is refractory to treatment, or the patient has refractory ascites or hepatorenal syndrome. Contraindications include polycystic liver disease, cardiac failure, hepatic encephalopathy, systemic infection, biliary obstruction and portal vein thrombosis. Complications are encephalopathy, block of the stent due to thrombosis and delayed shunt stenosis.

Supportive Care

- Avoid oral feeds—usually nutritional supplementation is not necessary.
- Posture—place the child on one side. If hypotension is present, foot end of the bed can be raised.
- Airway protection to prevent aspiration of blood, which is common in massive bleeding or unconscious patients.
- Maintain a normal plasma volume—the patient should be haemodynamically stable and the haemoglobin level should be more than 8 g/dL. This can be achieved by blood transfusion (20 mL/kg slowly), or administration of colloid solution. This should, however, be done with caution as blood transfusion increases the portal pressure and aggravate the bleeding, and may also result in

worsening of ascites.
- Corrective coagulopathy—fresh frozen plasma, clotting factors and vitamin K can be given, if indicated.
- Antibiotics are used to treat infections which may be associated with bleeding.
- Monitoring of a bleeding child—done by measurement of blood pressure and central venous pressure.

Treatment of the Primary Cause

The primary cause is identified and treated accordingly. Some examples are D-Penicillamine for Wilson's disease, genetic therapy for genetic disorders and surgical removal of obstruction.

COMPLICATIONS

These can be due to the varices or the treatment. Severe and persistent upper GI bleeding requiring more than 5 units of blood transfusion has an increased mortality rate. Some of the complications are given as follows:

1. Associated with GI bleeding
   - Vascular collapse
   - Arrhythmias
   - Aspiration
   - Sepsis
2. Associated with varices treated by sclerotherapy
   - Rebleeding
   - Oesophageal stenosis
   - Oesophageal ulceration
3. Related to blood transfusion
   - Over transfusion
   - Transmission of infection
4. Related to therapeutic procedures
   - Balloon tamponade is associated with aspiration pneumonia, oesophageal perforation, gastric mucosal lesions, pressure necrosis of mucosa.
   - Distal splenorenal shunting is associated with encephalopathy.
   - Complications of liver transplantation include transplant rejection, graft-versus-host disease.
5. Due to drugs—immunosuppressive drugs cause decreased immunity.

PROGNOSIS

Eighty per cent of the cases with variceal bleeding resolve spontaneously. Prognosis depends on the following factors:

- Course of the disease
- Severity of portal hypertension
- Location of varices
- Number of varices—the more the number, the poorer is the prognosis
- Grading of varices
- Severity of liver disease—Child–Pugh grade C carries poor prognosis
- Functional state of liver
- Rebleeding—early rebleeding within 5 days of admission carries poor prognosis
- Presence of complications is associated with poor prognosis
- Presence of associated systemic disorders
- Response to emergency treatment—children who respond poorly carry a poor prognosis.

PREVENTION

1. Primary prophylaxis/prevention—it refers to prevention of first bleeding from varices in a child with portal hypertension. The risk for bleeding and death is high in patients with oesophageal varices. Prevention of bleeding can be done by the following methods:
   - Reduction of portal venous pressure—β-blockers, somatostatin, vasopressin, etc.
   - Directly treating the varices by endoscopic variceal ligation (banding) or sclerotherapy
2. Secondary prophylaxis/prevention—it means prevention of recurrent bleeding in a child who has a history of variceal bleed. It can be done by the following methods:
   - Endoscopic sclerotherapy/or variceal ligation (banding)
   - Portosystemic shunt surgery—TIPS
   - Combination of endoscopic sclerotherapy or variceal ligation plus β-blockers and isosorbide-5-mononitrate

ASCITES

Ascites is an abnormal accumulation of fluid in the peritoneal cavity. The term *ascites* is of Greek origin. *Askos* means 'bag' or 'bladder'. The causes of ascites vary with age and differ among neonates and older children.

CLINICAL APPROACH

History Taking

The following points should be checked in a case of ascites:

- Abdominal discomfort due to abdominal distension
- Weight gain
- Dyspnoea (due to abdominal distension or associated pleural effusion)
- Site of onset of oedema—a part of the body where the collection of fluid occurred first. In cardiac failure pedal oedema is followed by ascites; while in cirrhosis, ascites is followed by pedal oedema.

General Examination

General examination findings are summarised in Table 10.48. These may give a clue to the cause of the diagnosis.

TABLE 10.48 General Examination Findings in a Case of Ascites

Clinical Findings	Probable Aetiology
Jaundice, palmar erythema, spider nevi	Possible hepatic cause
Elevated JVP	Cardiac cause
Left supraclavicular node (Virchow's node) enlargement	Gastric or upper abdominal malignancy
Firm nodule in the umbilicus (Sister Mary Joseph nodule)	Gastric, pancreatic or hepatic malignancy
Clubbing	Cirrhosis
Oedema	Pitting in cirrhosis, non-pitting in hypothyroidism
Tuberculous markers such as phlycten	Tuberculous abdomen

Abdominal Examination

Inspection

The clinician should look for the following during inspection of the abdomen in a case with ascites:

- Uniform distension of abdomen with fullness of flanks
- Umbilicus may be flushed with surface of the abdomen, everted or ballooned out
- Divarication of recti
- Tense and shiny skin of the abdomen
- Scrotal or penile oedema

Palpation

- Tense abdomen—the abdomen may be soft in the earlier stages of ascites when the fluid is minimal. The abdomen becomes tense with the progression of ascites
- Divarication of recti confirmed by palpation
- Direction of flow in dilated veins
- Deep palpation for organomegaly

Percussion

The presence of ascitic fluid in the abdomen can be tested by any of the following methods (described in detail in section *Percussion*, page 455):

- Dullness in the flanks—normally, the flanks should be resonant. However, in the presence of ascites the fluid gets collected in the flanks on lying supine. This results in dullness in the flanks.
- Shifting dullness—this test is positive only when the fluid collection is more than 1000 mL in older children and adults. In smaller children, this can be elicited even with lower amount of fluid.
- Puddle's sign (Lawson's sign)—puddle means small collection of water. This method can clinically detect even 100 mL of fluid in the peritoneal cavity.
- Fluid thrill—this is not as reliable as the above tests. With the child lying supine, place one hand on one side of abdomen. Ask the child or the attendant to place the ulnar side of his hand in the middle of the abdomen. A firm pressure should not be applied as this prevents the trans-

mission of the thrill. Now, the other side of the abdomen is gently tapped. A fluid thrill will be appreciated on the opposite side.

Fluid thrill and shifting dullness may be absent in ascites in the following conditions:

- Loculated ascites
- Peritoneal adhesions
- Tense ascites
- Minimal ascites

Auscultation

- Auscultopercussion—this is a combination of auscultation and percussion. It is used to detect minimal ascites. The child is put in a knee–elbow position for a few minutes to allow the fluid to collect around the umbilicus. The examiner then places the diaphragm of the stethoscope over the umbilicus and starts percussing towards the umbilicus. There is a change in the auscultatory tone once the percussion crosses the fluid level. This test can also be done by scratching the abdominal wall away from the umbilicus and observing the point where the auscultatory note changes.
- Bowel sounds are absent in peritonitis.
- Cruveilhier–Baumgarten syndrome—continuous murmur is heard over the umbilical area due to increased flow in the umbilical veins.
- Diminished breath sounds due to basal collapse on the lower part of the lung or hydrothorax on the right side or both sides.
- Succussion splash.

Per rectal Examination

During per rectal examination, a boggy, fluctuant mass can be felt due to the presence of fluid in the peritoneal cavity.

Abdominal Measurements

Clinical assessment of the progress of ascites is done by measuring the abdominal girth and weighing the patient daily. The measurement should be done daily in the same position either with the child standing or lying down at the level of the umbilicus.

PATHOGENESIS

Ascitic fluid may be transudate (with low protein concentration) or exudate (with high protein concentration). The mechanisms behind formation of ascitic fluid are as follows:

- Increased hydrostatic pressure in the portal vessels—this is associated with portal hypertension and promotes filtration of fluid from the blood vessels to the interstitial space. In CCF, the increase in venous pressure leads to obstruction of the vena cava, portal vein or lymphatic tract.
- Decreased oncotic pressure—this occurs due to increased protein loss from renal or GIT or decreased production by liver—ascites due to hypoalbuminaemia is due to this mechanism.
- Increased capillary endothelial permeability—this facilitates flow of fluid out of the capillaries and happens in inflammatory or neoplastic causes. For instance, ascites due to infection or inflammation of peritoneum (peritonitis) is due to this mechanism. The protein content is high in such cases.
- Stimulation of the renin–angiotensin–aldosterone system (RAAS)—this results from an increase in aldosterone and antidiuretic hormone (ADH) levels leading to sodium and water retention. This results in increased osmotic tension of interstitial fluid.
- Impaired lymphatic return or rupture of obstructed lymphatics into the peritoneum.

In many conditions more than one of these mechanisms act together to cause ascites. For example the mechanisms behind ascites seen in cirrhosis include

- Decreased colloid oncotic pressure due to hypoalbuminaemia caused by decreased production of albumin by the liver.
- Secondary hyperaldosteronism—as there is decreased effective circulatory volume and decreased renal blood volume, there is stimulation of RAAS leading to sodium and water retention.
- Impaired water excretion due to ADH. Decrease in effective circulating volume results in increased secretion of ADH.
- Antidiuretic hormone and renin angiotensin are not be metabolised by the failing liver. This results

in prolonged duration of circulation of ADH and renin angiotensin due to liver cell failure.
- Increased formation of hepatic lymph due to distortion and blockage of hepatic sinusoids and lymphatics on the liver surface. This predisposes to seepage of lymph through the liver capsule
- Fluid leak from visceral peritoneal capillaries.

Theories in Pathophysiology of Ascites

Many theories have been proposed to describe these mechanisms. Some of the popular theories include

- Underfill theory—there is an inappropriate increase of fluid in the splanchnic vascular bed which decreases the effective circulating blood volume. This activates the renin, aldosterone and sympathetic nervous system which predisposes to sodium and water retention. There is an increased hepatic sinusoidal pressure and low serum oncotic pressure. This forces fluid out into the interstitial space. The collection of fluid exceeds the capacity of lymphatics to reabsorb it, which results in ascites formation.
- Overflow theory—this theory states that there is retention of sodium and water even in the absence of hypovolaemia. This increases the hydrostatic pressure in the hepatosplanchnic circulation. This predisposes to extravasation of fluid into the peritoneal cavity and ascites formation. This was observed in children with cirrhosis who had hypovolaemia.
- Peripheral vasodilatation theory—it is the most recent theory which includes the components of other two theories. Portal hypertension is associated with splanchnic vasodilatation. There is a fall in effective blood volume due to arterial vasodilatation. This predisposes to renal sodium and water retention which results in expansion of plasma volume. This fluid overflows into the peritoneum.

Thus, this theory states that the underfilling occurs at the beginning and overflow in the later stages. Also, it is noted that nitric oxide synthase activity is greater in children with ascites as compared to normal children. Nitric oxide mediates splanchnic and peripheral vasodilatation.

ASSOCIATED PROBLEMS

- Accumulation of fluid in the peritoneal cavity results in disturbed haemostasis. This results in further salt and water retention which may precipitate hepatorenal syndrome.
- Ascitic fluid is a good media for infection.
- Pressure on the diaphragm results in decreased tidal volume and breathing difficulty.
- Accumulation of clotting factors in the ascitic fluid.
- Accumulation of albumin in the ascitic fluid.

ONSET

The onset of ascites gives a clue to the diagnosis. The onset can be acute or chronic. The causes of acute and chronic ascites are as follows:

1. Acute ascites
   - Peritonitis
   - Fulminant hepatic failure
   - Venous obstruction—IVC obstruction
   - Budd–Chiari syndrome
   - Splenic vein thrombosis
   - Portal vein thrombosis
2. Chronic ascites
   - Infections—tuberculous abdomen, pancreatitis
   - Hepatic causes—cirrhosis
   - Cardiovascular causes—constrictive pericarditis
   - Renal—nephrotic syndrome
   - GI causes—protein losing enteropathy
   - Neoplasms—lymphoma, neuroblastoma, ovarian tumours
   - Endocrine causes—hypothyroidism
   - Miscellaneous—chronic Budd–Chiari syndrome, chylous ascites

CLASSIFICATION BASED ON THE TYPE OF FLUID

Ascites can be classified based on the fluid composition. The main categories of ascites depending on the type of ascitic fluid include

I. Exudative (purulent)—due to infection in the

peritoneum

II. Transudative—due to hypoalbuminaemia
III. Chylous—obstruction or rupture of lymphatics predisposes to collection of lymph in the peritoneal cavity
IV. Haemorrhagic—secondaries in peritoneum are associated with collection of blood
V. Bilious—due to biliary tract obstruction
VI. Urinary—seepage of urine from distended bladder or from ruptured urethra results in collection of urine in the peritoneal cavity

Differentiating features between different types of ascites are given in Table 10.49 and differentiating features between ascitic fluid of cirrhosis and tuberculosis are given in Table 10.50.

CLASSIFICATION BASED ON THE SAAG OF FLUID

Earlier classification was based on the serum total proteins and was not useful in identifying the aetiological factors as the protein levels are altered in patients on prolonged diuretic therapy. Hence, the classification based on SAAG was found to be more useful (Table 10.51).

CAUSES

The causes of ascites are distinctively different in newborns and in older children.

Newborn

In newborns, ascites can be a component of hydrops or can appear independently. The causes of ascites as a part of hydrops are compiled in Table 10.52.

The collection of fluid in the peritoneal cavity can be seen in other conditions where the lymphatics or ureters rupture into the peritoneal cavity and lead to collection of lymph and urine, respectively. Ascites without hydrops in newborn may be due to the following causes:

- Chylous ascites—it is due to rupture of intestinal lymphatics. This may be due to malformation of mesenteric lymphatics or congenital obstruction of lymphatics at the level of cisterna chyli.

TABLE 10.49 Differentiating Features between Various Types of Ascitic Fluid

Features	Transudate	Exudate	Chylous	Pseudochyle	Haemorrhage	Urine	Bile
Appearance	Clear and colourless	Pink or white	Pale, straw or white	White	Red/pink	Clear to pale yellow	Slightly cloudy or yellow
Protein (g/dL)	<2.5	2.5–5.0	2.5–7.0	>2.5	>5.5	>2.5	>2.5
Specific gravity	<1.018	>1.018	1.007 to >1.040	1.007–1.040	1.007–1.027	1.010–1.040	1,010–1,011
Cell count/mm^3	<1.000	5,000–50,000	<10,000	<10,000	>50,000 RBCs	5,000–50,000	5,000–750,000
Cell type	Neutrophils, mesothelial cells	Neutrophils, mesothelial cells, macrophages, erythrocytes, lymphocytes	Neutrophils, mesothelial cells, small lymphocytes	Neutrophils, mesothelial cells, small lymphocytes	RBCs	Neutrophils, erythrocytes, macrophages, lymphocytes	Neutrophils, erythrocytes, macrophages, lymphocytes
Other features	Does not clot on standing	Often clots on standing	The fluid separates into cream-like layer when refrigerated. Fat droplets stain with Sudan III	Does not stain with sudan III. Does not separate into cream-like layer when refrigerated	Does not clot. On centrifugation, supernatant is clear and sediment is red	Smell of urine	Bilirubin present

TABLE 10.50 Differentiating Features between Ascitic Fluid of Cirrhosis and Tuberculosis

Features	Cirrhosis	Tuberculosis
Appearance	Clear	Straw coloured
Protein (g/dL)	<2.5	>5.5
Specific gravity	<1.016	>1.016
Cell count/mm^3	<250	>1000
Cell type	Mostly endothelial	>70% are lymphocytes
Other features	Transudative in nature	Exudative in nature. Centrifuged deposits may show acid-fast tuberculous bacilli

TABLE 10.51 Classification of Ascites Depending on SAAG and Ascitic Fluid Protein

Ascitic Fluid	SAAG	
	High	Low
High protein	Acute Budd–Chiari syndrome Cardiac ascites—constrictive pericarditis Ascites in hypothyroidism	Tuberculous ascites Peritoneal malignancy Chylous ascites Pancreatic ascites
Low protein	Cirrhosis liver	Nephrotic syndrome

- Biliary ascites—it is due to rupture of biliary tract and may be seen in EHBA or following percutaneous hepatic cholangiography.
- Urinary ascites—it may be due to intraperitoneal rupture of bladder which results in leakage of urine into the peritoneal cavity.
- Peritonitis following the perforation of gut or paracentesis.

Older Children

The peritoneum can be either normal or involved (Table 10.53). The conditions not involving peritoneum are as follows:

1. Cardiac causes—congestive cardiac failure, constrictive pericarditis, endocardial fibroelastosis, tricuspid stenosis, Ebstein's anomaly, tricuspid regurgitation
2. Vascular causes—veno-occlusive disease, Budd–Chiari disease, hepatic vein thrombosis

TABLE 10.52 Aetiological Causes of Hydrops Foetalis which are Associated with Ascites

Aetiological Classification	Causes
Cardiovascular system	Congenital heart block Ebstein's anomaly Hypoplastic left heart syndrome
Haematological	Homozygous α-thalassaemia Isoimmune haemolytic anaemia Osteopetrosis Fetofetal transfusion in twin-to-twin transfusion syndrome or fetomaternal transfusion
Chromosomal	Turner's syndrome Down's syndrome Edward's syndrome Patau's syndrome
Infection	TORCH infection Congenital syphilis
Renal	Congenital nephrotic syndrome
Pulmonary	Pulmonary lymphangiectasia, pulmonary hypoplasia Congenital cystadenomatoid malformation of lungs
Maternal causes	Toxemia Diabetes Severe anaemia
Placenta or cord	Chorioangioma
Miscellaneous	Wilm's tumour neuroblastoma

3. Hepatic causes—decompensated cirrhosis/hepatic failure, hepatic venous occlusion (Budd–Chiari syndrome), portal hypertension
4. Renal causes
   - Acute glomerulonephritis (AGN)
   - Chronic renal failure (CRF)
   - Nephrotic syndrome
   - Obstructive uropathy
   - Perforation or rupture of urinary tract
   - Postrenal dialysis
5. Nutritional causes—protein energy malnutrition resulting in hypoproteinaemia
6. Endocrine causes—hypothyroidism
7. Neoplastic
   - Primary—lymphoma
   - Secondaries in liver/peritoneum
8. GI causes

TABLE 10.53 Classification of Ascites Depending on the Peritoneal Involvement and SAAG

Peritoneum	Causes		
	SAAG <1.1 g/dL		SAAG >1.1 g/dL
Normal	Hypoalbuminaemia	Nephrotic syndrome Protein losing enteropathy, severe malnutrition with anasarca	Portal hypertension Cirrhosis Fulminant hepatic failure Hepatic metastases CCF Constrictive pericarditis Budd–Chiari syndrome Tricuspid regurgitation
	Portal pressure increased	Portal hypertension	
	Miscellaneous	Chylous ascites Nephrogenic ascites Bile ascites Pancreatic ascites Urinary ascites Ovarian diseases—Meig's syndrome	
Involved	Infection	Peritonitis due to bacterial, tuberculous, fungal, streptococcal infections Parasitic infections HIV-virus associated peritonitis	
	Vasculitis	Systemic lupus erythematosus Henoch–Schonlein purpura Eosinophilic ascites	
	Lymphatics	Peritoneal lymphangiectasia	
	Malignancy	Primary mesothelioma Peritoneal carcinomatosis hepatocellular carcinoma Secondaries in peritoneum	
	Miscellaneous	Granulomatous peritonitis Eosinophilic peritonitis	

- Chronic tuberculous peritonitis
- Pancreatitis
- Bowel infarction
- Perforation of bowel
- Protein losing enteropathy—chronic diarrhoea

9. Miscellaneous
   - Chylous ascites
   - Gynecological—Meig's syndrome associated with ovarian tumour
   - Lymphatic obstruction

Isolated Ascites

It is a condition where there is collection of fluid only in the peritoneal cavity. It is not associated with systemic disorders and collection of fluid in other parts. One of the following local causes should be searched for

- Chylous—lymphatic channel abnormality
- Biliary—spontaneous perforation of biliary tract
- Pancreatic duct anomaly
- Peritonitis—chemical, bile, meconium, bacterial

CLINICAL FEATURES

The salient clinical features of ascites include

- Uniform distension of the abdomen with fullness of flanks
- Tense shiny skin, abdominal striae (due to chronic stretching of skin)
- Puncture marks (in chronic ascites due to previous tapping of fluid)
- Umbilicus may be flushed with the surface of the abdomen or everted or may be ballooned out
- Divarication of recti
- The abdomen may be soft in the earlier stages when the fluid is minimal. When the ascites is more, the abdomen becomes tense
- Shifting dullness
- Fluid thrill

- Umbilical hernia
- Scrotal or penile oedema

ASSESSMENT OF SEVERITY

Assessment of the severity of ascites is important as it determines the course of treatment and predicts the complications and prognosis. The severity can be assessed by staging and grading of ascites. Ascites can be semiquantified as given in Table 10.54.

The grading of ascites is done as per Table 10.55.

TABLE 10.54 Semiquantification of Ascites

Semiquantification	Features
+	Detectable only by careful examination
++	Easily detectable but of relatively small volume
+++	Obvious ascites but not tense
++++	Tense ascites

TABLE 10.55 Grading of Ascites

Grade	Severity	Features
I	Mild	Puddle sign present. Ascites detected by USG
II	Moderate	Shifting dullness present. No fluid thrill
III	Severe	Tense ascites. Fluid thrill present Respiratory distress present

DIFFERENTIAL DIAGNOSIS

Ascites should be differentiated from the following conditions:

- Mesenteric cysts
- Ovarian cyst (Table 10.56)
- Peritoneal haemorrhage
- Distension of bladder
- Simple obesity
- Gastric dilatation
- Abdominal organomegaly or tumours

COMPLICATIONS

The complications of ascites include the following:

- Basal atelectasis of lungs due to pressure by the distended abdomen
- Variceal bleeding due to development of porto-systemic collaterals
- Cardiorespiratory distress
- Hepatic failure
- Gastro-oesophageal reflux
- Mesenteric vein thrombosis
- Hernia—umbilical hernia, inguinal hernia
- Hydrothorax (common on the right side)
- Hypoventilation due to compression of the lungs by the distended abdomen
- Hepatorenal syndrome—sequestration of fluid in the abdomen leads to additional retention of fluid by the kidneys due to stimulatory effect on

TABLE 10.56 Differences between Gross Ascites and Ovarian Cyst

Features	Gross Ascites	Ovarian Cyst
Pathophysiology	Collection of fluid in the peritoneal cavity	Collection of fluid in the ovary
Gender	Both males and females	Females
Abdominal distension	Uniform Umbilicus is at the midway between the xiphisternum and pubic symphysis	More distension of the lower part of the abdomen Umbilicus is nearer to the xiphisternum than the pubic symphysis
Direction of abdominal distension	Transverse	Towards the anterior direction
Border	No definite border	Upper border can be seen
Umbilical slit	Transverse	Vertical or drawn up
Flanks	Full, dull on percussion	Not full, resonant on percussion
Shifting dullness	Positive	Negative
Spino-umbilical length	Equal on both sides	More on the side of the ovarian cyst

aldosterone and sympathetic system. There will be increased renin secretion due to decreased renal perfusion. Decreased renal perfusion may predispose to renal failure
- Spontaneous bacterial peritonitis—fluid in the peritoneal cavity becomes a good ground for infections
- Prolapse uterus and rectum due to increased intra-abdominal pressure

INVESTIGATIONS

Investigations should be done to identify the type of fluid and the aetiological factors.

Ascitic Fluid Tap

Site

Ascitic fluid tapping is usually done at the following sites:

- Linea alba—this is a relatively avascular region and ideal for tapping. There is no muscle underlying this part of the abdomen. It is the thinnest part in the abdomen. Hence, it is easy to insert the needle in this part. Tapping through linea alba can be done at a point midway between umbilicus and pubic symphysis.
- Right iliac fossa—tapping can be done at the junction of upper one-third and lower two-thirds of the spinoumbilical line. This point is lateral to inferior epigastric artery. Any injury to the artery is, therefore, avoided. Tapping on the left side may result in injury to the rectum. Hence, tapping is done on the right side.

Procedure

The patient is asked to void urine before tapping and the site of tapping is selected. Local anaesthesia should be given at the site selected for tapping. A wide gauge needle or a trocar and canula is used for abdominal paracentesis.

After taking adequate aseptic precautions, the skin of the area is retracted by about 2 cm and the needle is inserted. After insertion, the needle is inserted in a Z-shaped tract to prevent fluid leakage from the local site. The tapping is done gradually. About 10–20 mL of fluid is withdrawn and sent for investigations. The needle is then removed slowly and the skin is released. This helps in sealing of the tapped site by the skin. The punctured site is also sealed with application of tincture benzoin.

Complications

The complications of ascitic fluid tapping include the following:

H	Hypovolaemia Hepatic failure
E	Encephalopathy—hepatic
P	Perforation of hollow viscus—bowel (occurs if tapping is done through the left iliac fossa) and bladder (occurs if tapping is done with full bladder)
A	Albumin loss (hypoproteinaemia)
T	Traumatic leakage of ascitic fluid from the tapped site
I	Infection—peritonitis
C	Cardiorespiratory distress Cardiogenic shock

Ascitic Fluid Analysis

The ascitic fluid should be analysed for the following:

1. Appearance—the appearance of the ascitic fluid can help detect the underlying condition (Table 10.57).
2. Specific gravity—it is defined as the ratio of the density of a given solid or liquid substance to the density of water at a specific temperature and pressure typically at 39°F and 760 mm Hg. Specific gravity is <1.016 in transudates and >1.016 in exudates.
3. Serum–ascitic albumin gradient (SAAG)—it is calculated by subtracting the ascitic fluid albumin value from the serum albumin value

   SAAG = serum albumin − ascitic fluid albumin.

   It is used for assessing the causes of ascites as this correlates well with the portal pressure. This is more useful than classifying the ascitic fluid as transudate or exudate. SAAG is determined by the oncotic and hydrostatic pressure. The gradient of ascites can vary depending on

TABLE 10.57 Appearance of Ascitic Fluid

Appearance of Ascitic Fluid	Condition
Clear, transparent and yellow tinged	Chronic liver disease Hypoproteinaemia Renal causes
Cloudy/turbid	Infections
Straw coloured	Tuberculous infections in the abdomen
Pink when the RBCs are >10,000/μL	Traumatic tap
Haemorrhagic (blood tinged when the RBCs are >20,000/μL)	Tuberculosis in the peritoneum Pancreatitis Malignancy Traumatic
Opaque/chylous	Lymphatic obstruction
Xanthochromic	Jaundice

the causative factors. High-gradient ascites (>1.1 g/dL) is associated with portal hypertension. High SAAG ascites with high protein >2.5 g/dL is seen in hepatic congestion. Low SAAG ascites (<1.1g/dL) with high protein is seen in cases associated with malignancy. Some conditions associated with high- and low-gradient ascites are listed in Table 10.58. Mixed ascites is seen when two or more causes result in ascites. The SAAG is high in these cases.

4. Cytology of ascitic fluid
   - Cell count
   - Malignant cells
5. Staining—the ascitic fluid should be stained (both gram's stain and acid fast staining) to detect the presence of microorganisms, if present.
6. Culture—the fluid should be cultured for acid fast bacilli (AFB).
7. Biochemical analysis:
   - Protein content—total protein and albumin content.
   - Amylase level in the fluid is elevated in pancreatitis and gut perforation.
   - Lactate dehydrogenase is increased in infections.
   - Glucose is low in infections.
   - Adenosine deaminase is increased in tuberculous infections.
   - Triglycerides are increased in chylous ascites.
   - pH of ascitic fluid is acidic in infections.

TABLE 10.58 Differences between High- and Low-Gradient Ascites

Features	High SAAG	Low SAAG
SAAG	Difference between ascitic albumin and serum albumin >1.1 g/dL	Difference between ascitic albumin and serum albumin < 1.1 g/dL
Pathogenesis	Increased pressure in the portal vein (portal hypertension) >8 mm Hg	Actively secreted fluid due to inflammation or malignancy (non-portal hypertension)
Lactic dehydrogenase	Low	High
pH	High	Low
Glucose	Normal	Low
WBCs	<1000/mm^3	>1000/mm^3
Causes	Hepatic causes with portal hypertension (cirrhosis, fulminant hepatic failure) Posthepatic causes (cardiac ascites, constrictive pericarditis, Budd–Chiari syndrome, veno-occlusive disease, portal vein thrombosis) Kwashiorkor Mixed ascites	Tuberculous peritonitis Nephrotic syndrome Pancreatic ascites Biliary ascites Connective tissue disorders Bowel obstruction or infarction Malignancy of peritoneum Hereditary angioedema

Other Investigations

The other investigations advised in ascites include

1. Ascitic fluid polymorph count—white blood cell count is more than 500 cells/mm^3 with >250 polymorphonuclear leucocytes/cm^3 in bacterial peritonitis. Lymphocytes are elevated in tuberculous peritonitis.
2. Red blood cell count is >50,000 cells/cm^3 in traumatic ascites.
3. Mantoux test.
4. Hepatitis viral markers—HBsAg, anti-HCV.

5. Liver function tests
   - Serum total protein is decreased due to decreased albumin production by liver.
   - Albumin to globulin ratio is reversed in children with liver cell failure due to decreased production of albumin. Also, there is an increased production of γ-globulins.
   - Liver enzymes are increased in children with inflammation, hyperadrenocorticism or gall bladder obstruction. SGOT is increased in hepatocellular and muscular injury. SGPT is a more specific test for liver cell injury. It may be more than 10 times elevated in hepatocellular jaundice. Liver enzymes are normal or low in children with impaired liver cell synthesis in the end stage liver disease.
   - Prothrombin time is increased in children with liver cell failure due to decreased vitamin K absorption. Vitamin K-dependent factors will be decreased.
   - Alkaline phosphatase is increased in cholestasis due to biliary obstruction.
   - 5'-Nucleotidase and GGT are increased when there is obstruction to bile flow.
   - Serum bilirubin is increased in liver cell damage, obstruction to the bile duct, gall bladder distension or obstruction or sepsis. The conjugated bilirubin fraction will be more than 15%–20% of the total bilirubin. When the jaundice is due to excessive haemolysis, and the bilirubin production exceeds the liver conjugating capacity, the unconjugated fraction will be more than 90%. A rise in bilirubin during treatment indicates that the child is not improving.
   - Blood cholesterol is low in liver cell failure.
6. Serum urea and creatinine are elevated in hepatorenal failure. These are decreased in children with impaired liver synthesis or hyperadrenocorticism.
7. X–ray of abdomen to detect fluid in the abdomen
   - Ground glass appearance, diffuse abdominal haziness, separation of small bowel loops, centralisation of floating gas containing bowel loop, indistinct psoas margins, bulging of the flanks.
   - Poor definition of intra-abdominal organs and margins of psoas muscle.
   - Separation of bowel loops by the ascitic fluid.
   - Hellmer's sign—the lateral edge of liver is displaced medially from the thoracoabdominal wall.
   - Medial displacement of caecum and ascending column by the ascitic fluid.
   - Dog ear sign—fluid in the pelvis accumulates in the rectovesical pouch, and then spills into the paravesical fossa. This fluid in the paravesical fossa produces symmetric densities on both sides of the bladder. This gives a dog's ear or Mickey Mouse appearance.
8. Chest X-ray
   - Elevation of the diaphragm due to fluid in the peritoneum
   - Sympathetic pleural effusions (hydrothorax) in children with massive ascites
9. Ultrasound of abdomen—it is a sensitive technique for detection of fluid in the peritoneal cavity.
   - Uncomplicated ascites appears as a homogeneous, anechoic pattern.
   - Ultrasound of the abdomen can detect ascitic fluid as low as about 100 mL (Table 10.59). The fluid collects initially in the posterior subhepatic pouch known as Morison pouch. Also, it may collect around the liver giving a sonolucent appearance.
   - In massive ascites, the small bowel loops lie on either side of the vertically floating mesentery. This gives an arcuate appearance.

TABLE 10.59 Minimum Amount of Fluid Needed to Test for Ascitic Fluid

Method Used to Test for Ascitic fluid	Amount of Fluid Needed (mL)
Diagnostic tap	10–20
Puddle sign	100–120
Shifting dullness	500
Fluid thrill	1000–1500
Ultrasonogram	100
CT scan	100

TABLE 10.60 Appearance of Ascitic Fluid in Various Types of Ascites

Type of Fluid	Appearance
Blood	Coarse internal echoes
Chyle	Fine internal echoes
Pseudomyxoma peritoni	Multiple septa
Tuberculous	Multiple septa

- The appearance of ascites varies with the type of fluid (Table 10.60).
- Dilated portal veins with direction of flow in portal vein away from the liver is seen in cirrhosis.
- Splenomegaly is seen in portal hypertension.
- Colour doppler study may show Budd–Chiari syndrome.

10. CT scan can detect about 100 mL of fluid in the peritoneum. The density of the ascitic fluid is less than that of abdominal viscera and more than that of fat. CT scan is helpful in detecting other types of fluid such as haemoperitoneum.
11. Liver biopsy—it helps in ascertaining the aetiology and is also of prognostic value.
12. Laparoscopy and peritoneal biopsy may reveal tubercles in ascites due to TB peritonitis.

TREATMENT

The treatment is aimed at relief of the pressure symptoms, treatment of the underlying disease and preventing further progression of the disease. Children with mild ascites can be treated as outpatient by salt restriction in addition to other measures. Those with moderate ascites can be treated with diuretics and paracentesis. Children with massive or large volume ascites and refractory ascites should be treated in a hospital.

Goals

- Weight loss of 0.5 kg/day in children with ascites
- Weight loss of 0.5–1 kg/day in children with ascites and peripheral oedema
- Maintain negative nitrogen balance—24-hour urinary sodium concentration should be measured. Sodium excretion more than 78 mmol/day indicates a negative nitrogen balance. Random urine sodium to potassium ratio more than 1 also indicates a negative nitrogen balance.

Medical Treatment

Most of the children improve with medical treatment. However, surgical intervention may be needed in few cases of refractory ascites. The medical treatment of ascites depends on the albumin gradient.

Low-Albumin-Gradient Ascites

Low-albumin-gradient ascites is not associated with portal hypertension. Hence, the treatment involves addressing the underlying cause only. The treatment of some specific causes of low-albumin-gradient ascites is given in Table 10.61.

High-Albumin-Gradient Ascites

High-albumin-gradient ascites is associated with portal hypertension. Hence, the treatment involves systemic stabilisation in addition to treatment of the underlying primary liver disease. Most of the patients improve with sodium restriction and diuretic therapy. The steps in treatment of high-albumin-gradient ascites are as follows:

1. Bed rest—this increases the plasma volume, improves the renal glomerular filtration and thereby causes diuresis. In upright position, there is an increase in renin–aldosterone activity which results in sodium and water retention.

TABLE 10.61 Treatment of Specific Causes of Low-Albumin-Gradient Ascites

Conditions	Treatment
Tuberculous ascites	Antituberculous treatment
Pancreatic ascites	Resolves spontaneously
Lymphatic ascites	Resolves spontaneously
Chalmydial peritonitis	Tetracycline
Nephrotic syndrome	Steroids
SLE	Steroids
Malignancy	Antimalignancy therapy

2. Diet—the food should contain the following:
   (a) Calories—provide 150% of the recommended daily allowance. If the daily requirement is 100 kcal/kg/day, give 150 kcal/kg/day
   (b) Proteins—15%
   (c) Fats—30%–35%
   (d) Carbohydrates—50%–60%
   (e) Sodium restriction—salt restriction is the mainstay of treatment. Sodium in the diet may be reduced to 20–30 mEq/day or 2–3 g/day
3. Intake/output chart—use of diuretics leads to loss of fluid from the intravascular compartment. This fluid is replenished from the fluid in the peritoneal cavity and results in weight loss. Fluid need not be restricted in all children with ascites. However, in children with persistent hyponatraemia (serum sodium level <130 mEq/L) the fluid intake should be reduced to less than three-fourths of the required amount.
4. Diuretics—spironolactone is the drug of choice. It blocks the aldosterone receptors in the collecting tubules and thus counteracts salt retention. Triamterene or amiloride can also be used.
   (a) Potassium sparing diuretics (spironolactone, triamterene, amiloride).
      - The diuretics of this class result in a negative fluid balance of 10 mL/kg/day.
      - Spironolactone is administered in the dosage of 2 mg/kg/day as a single dose in the morning.
      - Amiloride can be given in a dose of 5–20 mg/kg orally in four divided doses in older children and adults.

   (b) Loop diuretics are used in children with ascites not responding to spironolactone.
      - Furosemide acts by interfering with chloride binding cotransport system. It thus inhibits sodium and chloride reabsorption in the ascending loop of Henle. This is administered orally in the dosage of 1–2 mg/kg (up to a maximum of 6 mg/kg/day or 160 mg/day); 1 mg/kg can be administered intravenously. The dosage of diuretics can be increased until a negative sodium balance occurs. This is monitored by measuring the urinary sodium to potassium ratio. It is >1% in children with negative balance where the sodium excretion in the urine is more than 78 mmol/day.
      - Bumetanide or torasemide can also be used.

   (c) Combination of potassium sparing and loop diuretics is used to improve diuresis in children who do not respond to single drug therapy. Combination of these drugs is helpful as they act at different sites.
      - Spironolactone 1.5–3.5 mg/kg/day in four divided doses, up to a maximum of 6 mg/kg/day or 600 mg/day
      - Furosemide 1–2 mg/kg (up to a maximum of 6 mg/kg)

   (d) Thiazide diuretics—hydrochlorothiazide in the dosage of 2–3 mg/kg can be given when the response to the above drugs is not adequate.
   (e) Diuretic resistance occurs in many children. This is tested by giving 80 mg of furosemide intravenously to a child who was not on diuretic therapy in the past 3 days. The child is put on a diet containing 80 mEq of sodium/day. Measure the urinary sodium excretion over the next 8 hours. This is less than 50 mEq in resistant cases.
5. Fluid restriction is useful in cases with hyponatraemia. Water restriction is helpful in children with persistent hyponatraemia below 130 mEq/L.
6. Albumin infusion—simultaneous volume expansion is done by infusing 20% albumin.
7. Paracentesis—this refers to slow and continuous removal of the ascitic fluid from the abdomen using a 18–22 G needle. A total of 200–400 mL/kg of fluid is tapped slowly over 4–6 hours in large volume paracentesis.
8. Peritoneal shunt.
9. Treatment of the primary cause—the underlying causes such as portal obstruction should be corrected.

Surgical Treatment

Ascites refractory to medical treatment may be considered for surgical intervention.

Various surgical modalities are given below:

1. Ascites ultrafiltration and reinfusion—the ascitic fluid is removed from the peritoneum which is filtered and then reinfused through a peripheral vein.
2. Portosystemic shunting—TIPS is done under radiological guidance in cases with ascites resistant to diuretic therapy. A stent is placed through the right jugular vein into the hepatic vein. This results in connection between portal and systemic circulation. This procedure is more effective in controlling ascites than other shunt procedures, but it is associated with an increased risk of hepatic encephalopathy. Figure 10.26 describes the mechanism by which TIPS helps in ascites.
3. Liver transplantation—the indications are as follows:
   - Refractory ascites
   - Low SAAG ascites—this type does not respond to decreased salt intake and diuretic therapy
   - Requirement of repeated paracentesis
   - Failure of repeated paracentesis

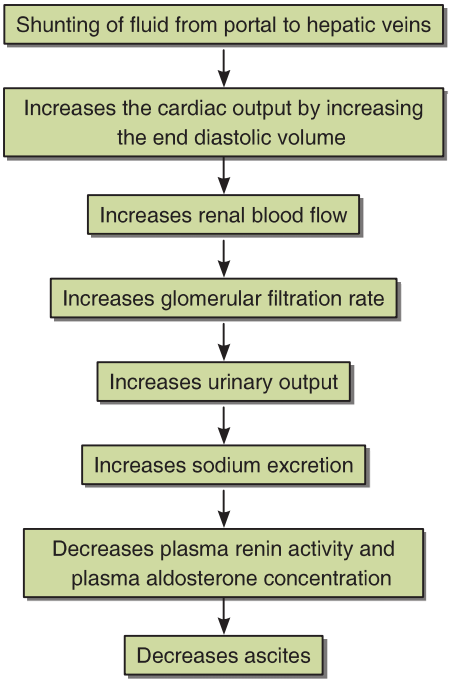


FIGURE 10.26 Role of TIPS in ascites.

MONITORING

Careful monitoring should be done in children with tense ascites or children treated with paracentesis. The response to treatment is assessed most commonly by monitoring the body weight. Optimal desirable decrease in the body weight is 0.5%–1% every 24 hours or 3%–5% within a week. Weight loss should not be more than 1 kg/day in children with ascites and pedal oedema, and not more than 0.5 kg/day in children with ascites only. The various other factors used to monitor the treatment are given in Table 10.62.

VARIANTS OF ASCITES

Refractory Ascites

When the ascites does not respond to the standard modes of treatment such as salt restriction and diuretics, or there is a requirement of repeated paracentesis, it is called refractory ascites.

TABLE 10.62 Monitoring and Follow-Up of Children on Treatment for Ascites

Daily			
Clinical	**Laboratory Tests**	**Alternate Day**	**Weekly**
Weight Abdominal girth Grading of ascites Pedal oedema	Serum electrolytes (sodium, potassium) Renal function tests (urea, creatinine)	Renal function tests (urea, creatinine) Prothrombin time Blood culture (non-enteric culture)	Liver function tests (total serum proteins, albumin, bilirubin, liver enzyme alanine aminotranferase SGPT)

Causes

Refractory ascites may be seen in the following conditions (Box 10.8):

- Hepatic causes—portal vein thrombosis, hepatic vein thrombosis, liver cell failure
- Infections such as tuberculosis in the abdomen
- Cardiac failure
- Renal failure
- Nutritional causes—malnutrition
- Malignancy in the peritoneum (secondaries in the peritoneum)
- Drugs—hepatotoxic drugs

Treatment

The treatment of refractory ascites includes

- Paracentesis—ascitic fluid tapping (of 100 mL/kg body weight) should be done at an interval of 2–3 weeks depending on the severity of sodium retention. A total of 200–400 mL/kg/day of ascitic fluid is removed in large volume paracentesis.
- Colloid replacement for volume expansion—for every litre of ascitic fluid removed, 6–8 g of 20% albumin is replaced.
- Peritoneo-jugulo-venous shunting (LeVeen shunt)—is used to shunt the ascitic fluid into the central venous system. The ascitic fluid is shunted from the peritoneum to the vessels such as SVC using a long tube. This is done in children with refractory ascites. The pressure in the peritoneal cavity is more than that in the venous system which facilitates the flow of ascitic fluid into the systemic circulation. Thus, fluid and protein loss is prevented. This results in increased flow to the heart. There is increased cardiac output, which increases the renal flow and glomerular filtration rate (GFR).

BOX 10.8 Predisposing factors of refractory ascites

F	Failure—cardiac, renal
L	Liver—hepatic vein thrombosis, liver cell failure
U	Undernutrition
I	Infection
D	Drugs—hepatotoxic

- Transjugular intrahepatic portosystemic shunt is placed between the portal and hepatic systems.
- Orthotopic liver transplantation is done for children with end-stage liver disease.
- Atrial natriuretic peptide is a substance secreted by the atrium when it is distended due to increased flow into the heart. This is a physiological mechanism by which fluid overload is prevented. It increases the GFR and causes natriuresis (salt and water excretion). Patients with advanced cirrhosis have a reduced response to atrial natriuretic peptide despite increased levels. Atrial natriuretic peptide can be tried along with terlipressin to counteract the hypotensive effect of atrial natriuretic peptide.
- Ultrafiltration and reinfusion of the ascitic fluid.

Recent Advances. Several drugs are under trial for treatment of refractory ascites. These include aquaretics which are vasopressin (V_2 receptor) antagonists and promote excretion of electrolyte free water. These are useful in patients with ascites and hyponatraemia.

Chylous Ascites

It is due to collection of fluid in the peritoneal cavity which is rich in lipid. This is more common in males. Leakage of chyle is common at the base of the superior mesenteric vessels but can be seen anywhere in the retroperitoneum or mesentery.

Causes

- Idiopathic (in neonates)
- Congenital malformations—small intestinal lymphangiectasis
- Infections—tuberculosis, pancreatitis
- Hepatobiliary diseases—storage diseases, neonatal hepatitis, viral hepatitis, α-1-antitrypsin deficiency
- Trauma resulting in disruption of the lymphatics or thoracic duct
- Compression of the lymphatics as in malrotation, hernia, intussusception and neoplasms

Investigations

1. Paracentesis—the findings are as follows:
   - Milky or turbid ascites; turbidity disappears on adding ether

- Fluid separates into two layers on standing
- Sudan staining positive for fat globules
- Increased triglyceride content (>1500 mg/dL) in ascitic fluid
- Lymphocytes >75%
- Proteins >3 g%

2. Ultrasonogram

Treatment

- The child should be given high protein and low fat diet (to compensate the protein loss in the ascitic fluid). Diet should, however, be rich in MCT as these can be directly absorbed into the blood stream and do not enter the lymphatic system. Most of the children who show slow response to dietary management recover with parenteral nutrition and bowel rest for 2–4 weeks.
- Paracentesis is required in massive ascites which causes cardiorespiratory problems.
- Surgical correction of the leak should be done in refractory ascites not responding to medical therapy even after 6 weeks. Exploratory surgery or laparoscopic intervention is useful in such cases.
- Peritoneovenous shunt may be required in few cases which do not improve with surgical repair.

Prognosis

The mortality rate for idiopathic neonatal chylous ascites is high.

Pseudo-Chylous Ascites

In certain conditions (such as chronic pancreatitis and persistent ascites), the fluid may appear turbid even without the presence of fat globules. These conditions are known as pseudo-chylous ascites. The turbidity in these conditions may be due to degeneration of the cells such as leucocytes. The differences between chylous and pseudo-chylous ascites are given in Table 10.63.

TABLE 10.63 Differences between Chylous and Pseudo-Chylous Ascites

Features	Chylous Ascites	Pseudo-Chylous Ascites
Aetiology	Rupture of lymphatic duct or thoracic duct	Long-standing ascites Chronic pancreatitis
Staining for fat (Sudan black)	Fat globules stain	Not stained
Ether test	Top layer of fluid becomes clear	Turbidity persists
Alkali test	No change	Turbidity clears as cellular proteins are dissolved
Triglycerides in the fluid	Elevated >1000 mg%	Not elevated
Cholesterol	Not elevated	Elevated
Treatment	Low-fat diet (low long chain triglycerides and high medium chain triglycerides) High protein diet Paracentesis Surgical correction of the leak	Treatment of the cause

Haemorrhagic Ascites

It is a condition where the ascitic fluid is blood-tinged. This is seen in the following conditions:

- Abdominal trauma
- Bleeding diathesis
- Tuberculous peritonitis
- Malignancy—primary abdominal malignancy or secondaries in the peritoneum

Biliary Ascites

It is rare in the newborn period. It is common under the age of 3 months but can occur at any age. It is due to spontaneous rupture of the bile duct, usually at the junction of the common bile duct and the cystic duct. The predisposing factors for the rupture are as follows:

- Intraductal pressure of the bile duct is elevated
- Congenital weakness of the wall of the bile duct
- Vascular insufficiency at the biliary ductal wall
- Pancreatic reflux
- Perforation of choledochal duct
- Trauma to the bile duct
- Iatrogenic after cholecystectomy

Clinical Features

- Distended abdomen due to ascites
- Mild jaundice (due to increased direct bilirubin)

Investigations

- Hepatobiliary scanning with iminodiacetic acid (IDA)—there is extraductal extravasation of the dye into the peritoneal cavity
- Ultrasonogram of abdomen—obstructive lesions or congenital anomalies may be seen
- Abdominal paracentesis—bilirubin in the peritoneal fluid

Treatment

- Surgical drainage either open or laparoscopic
- Intraoperative cholangiography with simple drainage

Prognosis

The perforation gets sealed spontaneously within a few weeks. No attempt should be made to repair or reconstruct the bile duct.

Pancreatic Ascites

Causes

- Abdominal trauma
- Acute or chronic pancreatitis

Features

Fluid is pigmented due to action of pancreatic enzymes on the erythrocytes.

Investigations

- Paracentesis—amylase level increased
- Ultrasonography
- CT scan

Treatment

- Bowel rest
- Total parenteral nutrition
- Administration of somatostatin analogues
- Endoscopic stents—endoscopic retrograde cholangiopancreatography with or without nasopancreatic transampullary stenting
- Explorative surgery with repair should be done if the condition does not improve with the above measures

Urinary Ascites

It is characterised by the collection of urine in the peritoneal cavity. It is common in males in the intrauterine period or under the age of 1 month. Urinary ascites due to traumatic rupture of urinary tract can occur at any age.

Causes

- Rupture of intraperitoneal bladder or ureters following the injury or surgery.
- Rupture of upper urinary tract into the peritoneal cavity. Posterior urethral valve, which is common in males, is a predisposing factor.
- Rupture of congenital bladder diverticula.
- Urinary tract anomalies such as cloaca predispose to reflux of urine through the genital tract into the peritoneal tract. During development the cloaca is separated into rectum and urogenital sinus by a septum. When it is not separated it persists as cloaca.

Clinical Features

- Abdominal distension
- Potter facies—large low set ears, flat face, recession of chin. This occurs in the intrauterine period. (When urine leaks into the peritoneal cavity, oligohydramnios occurs resulting in compression of face against the walls of uterus.)

Investigations

- Arterial blood gas (ABG)—acidosis
- Blood urea nitrogen (BUN) elevated
- Serum creatinine elevated
- Electrolyte abnormalities
- Paracentesis—creatinine levels elevated
- X-ray—voiding cystourethrography (VCUG) is helpful in identifying the site of urinary leak
- Ultrasonogram of abdomen

Treatment

1. Medical
   - Correction of electrolyte abnormalities
   - Rehydration
   - Antibiotics

2. Surgical
   - Catheter bladder drainage
   - Urinary tract decompression
   - Cystoscopic ablation of posterior urethral valve
   - Drainage of upper urinary tract may be necessary
   - Treated by surgical correction of the defect or obstruction

Iatrogenic Ascites

Causes

- Gastric perforation from gastric catheters
- Leakage of parenteral fluid given by umbilical cord catheterisation

Treatment

The treatment includes surgical exploration and repair.

Other Variants of Ascites

Ascites Praecox

Ascites due to constrictive pericarditis usually appears before the appearance of generalised oedema. It is also out of proportion to oedema in other parts of the body.

Purulent Ascites

It is a condition where pus is present in the ascitic fluid. This is caused by pyogenic peritonitis, ruptured amoebic liver abscess, etc.

HEPATIC FAILURE

It is a condition in which there is an impairment of functions of the liver cells. This can occur either due to destruction or due to functional impairment of liver cells.

CLASSIFICATION

Liver failure can be classified as hyperacute, acute and subacute on the basis of duration of coagulopathy. This was proposed by the Second World Congress of Pediatric Gastroenterology, Hepatology and Nutrition. Emphasis is placed on the presence of coagulopathy in the absence of sepsis or disseminated intravascular coagulation (DIC). This is because other features of liver failure may be absent, late or unrecognised in children. This coagulopathy is not correctable by parenteral administration of vitamin K within 8 hours.

I. *Hyperacute live failure* is defined as coagulopathy due to acute liver dysfunction of up to 10 days total duration by clinical criteria. This type is seen in paracetamol toxicity.
II. *Acute liver failure* is defined as coagulopathy due to acute liver dysfunction of more than 10 days total duration but less than 30 days by clinical criteria. Encephalopathy may be absent or not recognised especially in children. If this presents with encephalopathy, the prognosis is poor.
III. *Subacute liver failure* is defined as coagulopathy due to acute liver dysfunction of more than 31 days total duration but less than 6 months by clinical criteria. This condition always presents with jaundice and encephalopathy. It is seen in Wilson's disease, autoimmune hepatitis and following the drug-induced hepatotoxicity.

HISTORY TAKING

Presenting Complaints

The common symptoms in a child with hepatic failure are as follows:

- Lassitude
- Anorexia
- Delay in menarche
- Pale or clay-coloured stools (Fig. 10.27)
- Pain in abdomen, vomiting, constipation
- Fever
- GI bleeds—haematemesis, melaena, haematochezia
- Foetor hepaticus
- Pruritus

History of Present Illness

- H/o altered sensorium
- H/o jaundice



FIGURE 10.27 Clay-coloured stools in a newborn child. The child was later diagnosed as a case of extrahepatic biliary atresia.

- H/o vomiting, diarrhoea and constipation, which precipitate hepatic failure
- H/o oliguria (hepatorenal failure)
- H/o bleeding—haematemesis or haematochezia (due to varices or haemorrhoids)
- H/o altered sleep pattern (inversion of sleep rhythm)

History of Past Illness

- H/o jaundice
- H/o tattooing
- H/o unprotected sex—sexual contact with carriers of hepatitis B is important in adolescents and adults

Treatment History

- H/o needle pricks
- H/o blood transfusions
- H/o hepatotoxic drugs such as diazepam
- H/o surgery
- H/o tapping of large volume of ascitic fluid

Family History

- H/o Liver diseases and jaundice (genetic disorders)

CLINICAL EXAMINATION

The features of hepatic failure are as follows:

1. Breath—foetor hepaticus (due to mercaptans)
2. Head—alopecia or hair loss
3. Face
   - Hepatic facies/cirrhotic facies—hollow temporal fossa, shrunken eyes, parched lips, parotids enlarged, pinched up nose, icteric conjunctiva, muddy complexion of skin.
   - Spider naevi—dilated central arteriole and its radiating branches, so called as it resembles a spider. These are seen on the face and right side of the upper chest, which is drained by SVC. This dilatation of the vessels is due to the circulating oestrogens, which are not metabolised by the failing liver.
4. Eyes
   - Jaundice
   - Pallor
   - Signs of vitamin A deficiency—Bitot's spots, corneal/conjunctival xerosis or ulcer
   - Kayser–Fleischer ring if associated with Wilson's disease
   - Subconjunctival haemorrhage (vitamin K deficiency)
5. Upper limbs
   - Asterixis (flapping tremor)—outstretching of arms and dorsiflexion of wrist results in jerky forward movements of hand
   - Clubbing
   - Dupuytren's contracture (fibrosis of palmar aponeurosis due to released free radicals causes flexion deformities in the ring and little finger with flexion at metacarpophalangeal [MCP] joints)
   - Palmar erythema (due to the circulating oestrogens, which are not metabolised by the failing liver)
   - Nails—leukonychia (white nails due to hypoalbuminaemia)
6. Lower limbs
   - Oedema
   - Chronic leg ulcer
7. Skin
   - Bleeding—bruising/petechiae/ecchymosis (due to decreased vitamin K–dependent clotting factors 2, 7, 9 and 10)
   - Jaundice

- Paper money skin
- Phrynoderma—signs of vitamin A deficiency
- Scratch marks—due to itching may be seen in chronic cholestasis
- Look for markers of tuberculosis
- Slate grey skin in haemochromatosis

8. Chest
   - Axillary hair loss
   - Alopecia—loss of hair in the body
   - Breast atrophy (in females)
   - Breast enlargement (gynaecomastia) in males
   - Spider naevi
9. Abdomen
   - Abdominal distention/ascites
   - Shrinking liver size
   - Dilated veins—caput medusae
   - Tap marks/plasters after tapping is performed for ascites
10. External genitalia
    - Testicular atrophy
    - Loss of secondary sexual characters (loss of pubic hair)
11. Cardiovascular and respiratory system
    - Cardiorespiratory failure—hyperkinetic circulation, tachyarrhythmia
    - Tachypnoea initially followed by respiratory failure in stage IV coma
12. Neurological system
    - Neurological instability
    - Changes in personality
    - Altered sensorium/stupor/coma
    - Decerebrate rigidity
    - Changes in sleep pattern
13. Metabolic changes
    - Hypoglycaemia
    - Acid–base imbalances
    - Infections are associated with fever, leucocytosis, oliguria, acidosis, DIC
14. Associated features
    - Hepatorenal failure
    - Signs of fat-soluble vitamin deficiency A, D, E, K—the absorption of fat depends on the presence of bile in the intestine. In liver failure, the absorption of the bile is affected; hence, the absorption of the fat-soluble vitamins (vitamins A, D, E and K) is affected, giving rise to the deficiency symptoms

The pathogenesis of these clinical features is discussed in Table 10.64.

COMPLICATIONS

The complications of hepatic failure can be seen in many organs. Table 10.65 gives the common complications seen in hepatic failure.

Hepatopulmonary Syndrome

It is characterised by development of respiratory complications in a child with hepatic failure. Hepatopulmonary syndrome includes a triad of hypoxaemia, intrapulmonary vascular dilatations and liver disease. There is intrapulmonary right-to-left shunting of blood. The clinical features include hypoventilation, respiratory depression and exercise intolerance. This condition can be treated by mechanical ventilation.

Hepatorenal Failure

If renal failure occurs in a child with liver failure, it is called hepatorenal failure. The child presents with oliguria (urine output <1 mL/kg/hour). Renal function tests are deranged with rising blood urea and creatinine. Serum creatinine values are more than 1.5 mg/dL. Creatinine clearance is <40 mL/minute. Blood urea nitrogen may be normal or even decreased due to decreased synthesis by the failing liver. Acute sodium retention results in hypernatraemia. Urinary sodium is less than 20 mEq/L. Urine osmolality is more than plasma osmolality.

Treatment consists of expansion of plasma volume with albumin or fresh frozen plasma. Nephrotoxic drugs should be avoided. Dialysis is helpful. Liver transplantation may be done if required.

TABLE 10.64 Pathogenesis of Clinical Features in Patients with Hepatic Failure

Clinical Features	Pathogenesis
Altered consciousness/deterioration in level of consciousness/drowsiness/stupor/coma	Accumulation of toxic products (ammonia, neurotransmitters such as serotonin, catecholamine, glutamate, aspartate) in the circulation Accumulation of GABA has an inhibitory effect on the brain Production of false neurotransmitters Decreased cerebral blood flow and impaired cerebral autoregulation
Alopecia—loss of hair in the body	Due to defective synthesis of proteins
Breast atrophy (in females)	Decreased oestrogen levels
Bleeding (gastrointestinal)—haemetemesis, melaena	Superficial erosions (commonest) Portal hypertension with portosystemic collaterals (rare in children)
Coagulopathy (haemorrhage, petechiae, purpura)	Decreased absorption of vitamin K Deficiency of liver-dependent coagulation factors, i.e., 2, 5, 7, 9 and10 and anticlotting factors which are vitamin K dependent Altered platelet number and function DIC
Clubbing	Hypoxia due to development of arteriovenous fistula
Dupuytren's contracture	Fibrosis of palmar aponeurosis due to release of free radicals. This causes flexion deformities in the ring and little fingers with flexion at MCP joints. This is more common in alcoholic cirrhosis
Flapping tremor (asterixis)	Irritability of nerves due to accumulated toxic products which are not detoxified by the failing liver
Foetor hepaticus (mosty odour of the breath)	Due to mercaptans (methionine converted into methyl mercaptans)
Fluid retention	Decreased intravascular colloid osmotic pressure Renal retention of salt and water Hyperaldosteronism
Gynaecomastia	Oestrogens increased as it is not metabolised by failing liver
Hepatic facies—parched lips, muddy skin, icteric conjunctiva, enlarged parotids	Wasting of tissues and muscles in the face
Handwriting altered	Accumulation of toxic products
Infections—sepsis Increased susceptibility to infections (pneumonia, septicaemia, urinary tract infections and spontaneous bacterial peritonitis)	Altered immunity Neutropenia Impaired neutrophils and Kupffer cell phagocytic function Defective chemotaxis Reduced complement levels Defective opsonisation and loss of opsonin Loss of properdin
Jaundice	Decreased capacity of liver to conjugate bilirubin
Leukonychia—white nails	Hypoalbuminaemia due to decreased synthesis by liver
Malnutrition and hypoglycaemia	Impaired gluconeogenesis and glycogen storage
Neuropsychiatric manifestations	Accumulation of toxic products
Opisthotonus	Hepatic encephalopathy
Parotid swelling	Due to wasting of the surrounding tissues, the parotids appear falsely enlarged.
Pruritis	Cholestasis—increased bile acids

(Table continued)

TABLE 10.64 *(Continued)*

Clinical Features	Pathogenesis
Palmar erythema (liver palms)	High level of circulating oestrogens
Quiescent—become inactive, dormant and quiet or quieter than before in the presence of hypoglycaemia	Hypoglycaemia which is due to reduced insulin degradation, increased glucose utilisation, Decreased glucose synthesis by liver
Reduced liver span	Cirrhosis of liver
Spider naevi—central arteriole and its radiating branches are dilated	High level of circulating oestrogens
Secondary sexual characters lost Loss of body, axillary and pubic hair	Decreased testosterone/oestrogen receptors
Sleep rhythm altered (reversal of day and night sleep pattern)	Accumulation of toxic products (benzodiazepine-like substances) inhibit reticular activating system
Scratch marks	Itching in chronic cholestasis
Testicular atrophy	Oestrogens not metabolised by failing liver
Terry nails proximal half is white, distal half is brown red	Due to hypoalbuminaemia
Uraemia Urine output—decreased <1 mL/kg/hour	Hepatorenal syndrome Hypotension
Vitamins A, D, E and K deficiency symptoms	Fat malabsorption—hence fat-soluble vitamins not absorbed
Volume of pulse high	AV fistula Vasodilators increased—PGE1, PGE2, PGI2 Increased gastrointestinal peptides (VIP) Substance P
Wasting—muscle wasting	Impaired gluconeogenesis and glycogen storage
Warm hands	Increased oestrogen levels
Xanthomata Xanthelasma of eye lids	Lipid deposition in the dermis, subcutaneous tissue over the eyelids

INVESTIGATIONS

1. To find out the severity of liver failure
   - Urine for bile salts and bile pigments
   - Liver function tests—prothrombin time, total proteins, albumin, globulin, serum bilirubin, liver enzymes (ALT, AST, alkaline phosphatase, γ-glutamyl phosphatase) and cholesterol
2. To evaluate the complications
   - Hepatorenal syndrome—serum electrolytes, urea and creatinine
   - Hypoglycaemia—glucose reduced in liver disease
   - Hepatic encephalopathy—ammonia level elevated; electroencephalogram shows triphasic waves
3. To find the precipitating factors
   - Evidence of infection—blood culture is positive. Infections are associated with fever, leucocytosis, oliguria, acidosis and DIC
4. To find the aetiology
   - Viral hepatitis—viral markers such as HBsAg, anti-HBc, HBV-DNA, anti-HCV
   - Wilson's disease—serum ceruloplasmin, urinary copper, slit-lamp examination for KF ring
   - Haemochromatosis—serum iron and transferrin
   - Cystic fibrosis—sweat chloride
   - GSD—serum lactate and pyruvate

TABLE 10.65 Complications of Hepatic Failure

System	Complications
Neurological	Encephalopathy Cerebral oedema Altered consciousness/drowsiness/stupor/coma Seizures or fits Encephalopathy Cerebral oedema
Cardiovascular	Hypotension Warm shock Decreased peripheral resistance
Pulmonary	Respiratory acidosis, respiratory failure, tachypnoea initially, respiratory failure in stage IV coma. Respiratory failure is due to development of AV fistula
Metabolic	Hypoglycaemia
Electrolyte imbalances	Hyperkalaemia Hypokalaemia Hyponatraemia (dilutional)
Acid–base imbalance	Respiratory alkalosis (hyperventilation in early stage of hepatic encephalopathy) Metabolic alkalosis Respiratory acidosis
Endocrine	Increased testosterone and oestrogen levels
Haematological	Coagulopathy Disseminated intravascular coagulation-
Gastrointestinal	Haemorrhage
Renal	Renal failure Hepatorenal syndrome
Nutritional	Malnutrition, fat malabsorption—fat-soluble vitamins deficiency
Skeletal	Rickets
Miscellaneous	Cholestasis Ascites Haemodynamic instability Hypotension Hypoxia Jaundice

- α-1-Antitrypsin deficiency—α-1-antitrypsin level
- Metabolic disorders—urine screening tests for metabolic disorders
- Autoimmune hepatitis—autoantibodies (ANA, ASMA, AMA, LKM1 antibodies)
- TORCH infections—TORCH screening
- Hepatic cell injury—liver biopsy

TREATMENT

1. Supportive
   (a) Airway protection.
   (b) Endotracheal intubation and assisted ventilation and supplemental oxygen if there is respiratory failure, grade III or IV failure, shock hyperventilation to decrease cerebral oedema.
   (c) Catheterise the bladder.
   (d) Nasogastric aspiration using a nasogastric tube gastric wash with saline to remove GI bleeds.
   (e) Head end should be raised to 30°.
   (f) Intravenous fluids should be given with 10% dextrose.
   (g) Infections/sepsis—broad spectrum antibiotics.
   (h) Haemodialysis—indications are severe hyperkalaemia, severe acidosis, cerebral oedema and renal failure.
2. Dietary treatment—diet should contain optimal proteins and calories.
   (a) Protein 0.5–1 g/kg/day of branched chain amino acids are preferred. Albumin infusion is given if the serum albumin is falling rapidly. In grades I and II hepatic encephalopathies, normal protein intake is advised. In grades III and IV hepatic encephalopathies, 60%–80% of normal intake is advised. Vegetable proteins are preferred as they are less aminogenic.
   (b) Calories 150%–200% of the recommended daily allowance as these children are in a state of hypercatabolic state. Glucose 10% can be infused.
   (c) Fats should provide 35%–50% of the required calories. Medium chain triglycerides (coconut oil) are preferred as they are directly absorbed in the portal circulation and reduce steatorrhoea. Essential fatty acids (corn/safflower oil) and lipid solutions should be added.

(d) Supplementation of calcium, phosphorus and magnesium may be required.
(e) Fat-soluble vitamins A (3000–10,000 IU/day), D (400–4000 IU/day), E (50–400 IU/kg/day oral or 1–2 mg/kg/day intramuscular) and K (oral or parenteral) should be given if there is deficiency.

3. Treat the primary cause—specific therapy for hepatitis B, hepatitis C, Wilson's disease, tyrosinaemia, etc., should be given (Table 10.66).
4. Avoid the precipitating factors—the factors which precipitate liver failure should be avoided. These include drugs (thiazide diuretics, morphine, barbiturates), sedation, high protein diet (vegetable protein should be preferred), hypoxia, hypoglycaemia, GI bleeding, infections and electrolyte imbalance. Also, avoid tapping of fluid rapidly or in high volumes. Surgery or trauma should also be prevented.
5. Hepatic support
   (a) Plasmapheresis
   (b) Extracorporeal blood cleaning
   (c) Liver-assist devices for removing toxins (under trial)
   (d) Liver transplantation
6. Treatment of complications
   (a) Hepatic encephalopathy (see section *Treatment*, page 524)
   (b) Cardiovascular complications—parenteral fluids or colloid transfusion are given for haemodynamic instability. Hypotension should be treated with intravenous fluids and dopamine/dobutamine infusion, as required.

TABLE 10.66 Specific Therapy for Primary Cause in Liver Failure

Conditions	Treatment
Wilson's disease	Penicillamine
Paracetamol poisoning	Gastric lavage Start *N*-acetylcysteine within 24 hours of ingestion and continue until the liver failure resolves
Galactosaemia	Stop feeds containing galactose
Haemochromatosis	Desferrioxamine

(c) Respiratory complications—these include hypoxia, respiratory acidosis and respiratory failure. Treatment consists of the following:
- Oxygen (by mask in early stages and ventilation in Grades III and IV hepatic encephalopathies)
- Assisted ventilation
- N-acetylcysteine infusion improves oxygenation
- Hyperventilation (in Grades III and IV hepatic coma)
- Packed cell transfusion to maintain haemoglobin above 10 g/dL to improve oxygen carrying capacity
- Mild hypothermia (decreases oxygen demand)
- L-ornithine-L-aspartate (LOLA) infusion
- Albumin infusion may be helpful

(d) Metabolic complication—hypoglycaemia is corrected by parenteral fluids containing 10% dextrose.
(e) Electrolyte imbalances
- Hyponatraemia (dilutional) is treated by free water restriction, intravenous furosemide or bolus of hypertonic sodium chloride in severe cases
- Hyperkalaemia—haemodialysis
- Hypokalaemia—potassium supplements

(f) Haematological complications
- Coagulopathy—fresh frozen plasma, vitamin K and platelet transfusion are given if platelet count is <20,000 cells/mm^3.
- Disseminated intravascular coagulation—replacement therapy by infusion of cryoprecipitate or fresh frozen plasma. Treat the precipitating causes.

(g) GI bleed
- Antacids/H2 receptor blockers
- Ranitidine intravenously
- Installation of surface coagulants

(h) Kidney failure—renal dysfunction is treated by the following measures:

- Adequate fluid using colloid or plasma followed by diuretics
- Dialysis may be needed if renal failure is established
- Haemodialysis (correct hypo-osmolality with mannitol before haemodialysis)
- Low dose dopamine (2–5 µg/kg/day)
- Furosemide (1–2 mg/kg 6 hourly)
- Treat infections
- N-acetylcysteine

(i) Miscellaneous complications

- Cholestasis is treated by use of phenobarbitone 3–10 mg/kg/day. Phenobarbitone induces liver enzymes and promotes excretion of toxic products. Cholestyramine 250–500 mg/kg/day binds the bile salts. Antihistamines and ursodeoxycholic acid 10–15 mg/kg/day are also given.
- Ascites—fluid and sodium restriction, diuretics (spironolactone and furosemide), albumin infusion, paracentesis, peritoneovenous shunt.

MONITORING

The children with hepatic failure should be monitored periodically during treatment for the following:

- Intracranial pressure for cerebral oedema and cerebral perfusion pressure
- Infections—sepsis, pneumonia, peritonitis, urinary tract infections and so on
- Renal dysfunction due to renal tubular necrosis or hepatorenal syndrome

Monitoring protocol for a child with hepatic failure is given in Table 10.67.

TABLE 10.67 Monitoring Protocol in Hepatic Failure

Interval	Parameters
Every 4 hourly	Vital signs
Every 8 hourly	Intake/output monitoring
Every 12 hourly	Neurological grading Sodium Potassium Blood sugar ABG
Daily	PT
Weekly	Liver function tests Urea Creatinine Calcium and phosphorus

TABLE 10.68 Warning Signs in Acute Liver Failure

Parameters	Warning Signs
Clinical	Persistent anorexia Deepening jaundice Relapse of jaundice Shrinking liver size Spontaneous bleeds
Laboratory	Prothrombin time >5 seconds Persistent hypoglycaemia/low serum albumin Raised SGPT >3000 IU/L Serum bilirubin >20 mg/dL

WARNING SIGNS IN ACUTE LIVER FAILURE

In any child with chronic liver disease, various clinical and laboratory changes as given in Table 10.68 should alert the medical attendant. These manifestations are followed by acute liver failure and worsening of the patient. The child should be managed actively so that the progression of symptoms can be arrested. If no active treatment is given, the child develops encephalopathy.

PROGNOSIS

It depends on various static and dynamic factors. The static factors include the patient's age and aetiology. The dynamic factors refer to the development of complications, cerebral oedema, stage of encephalopathy, infections, PT and the level of serum bilirubin. Good and bad prognostic factors are given in Boxes 10.9 and 10.10.

FULMINANT HEPATIC FAILURE

It refers to the clinical syndrome of coagulopathy and encephalopathy which develops as a consequence of severe liver cell injury or functional impairment of liver cells. This disease usually evolves over a period

BOX 10.9 Good prognostic markers

- Appetite—early return of appetite
- Bleeding symptoms absent
- Cheerful and active child
- Decrease in transaminases—rapid fall in transaminases by 2 week with clinical improvement
- Enlarged palpable liver during prodrome
- Fever—rapid resolution of prodrome (fever/vomiting)
- Grade of coma I and II
- Hepatitis A infection
- Improvement—clinically
- Jaundice—early clearance of jaundice

BOX 10.10 Bad prognostic indicators

- Age >6 years and <10 years
- Causative agent—infections with non-A, non-B, non-C hepatitis, acute onset Wilson's disease
- Non-return of appetite by second week
- Serum bilirubin level >18 mg/dL (>300 µmol/L)
- Profound hypotension
- Cholestasis (marked) in the remaining parenchyma
- Duration of jaundice >1 week before the onset of encephalopathy
- Drug overdose
- Encephalopathy
- Electrolyte imbalance—hyponatraemia—persistent (serum Na^+ <125 mEq/L) serum K^+ >5.5 mEq/L
- Factor V level <20%
- Fits
- Gastrointestinal haemorrhage
- Persistent hypoglycaemia—blood glucose <45 mg/dL
- Hepatic coma grade III or more
- Jaundice level—bilirubin level >18 mg/dL (>300 µmol/L)
- Liver size—rapid reduction in liver size without clinical improvement
- Metabolic acidosis
- Multiorgan failure, associated respiratory failure
- Prothrombin time—prolonged PT >50 seconds (>8 seconds over control)
- Prolonged prodrome (fever/vomiting)

of 8 weeks from the onset of precipitating illness in patients without preexisting liver disease. This results from sudden and severe impairment of synthetic, excretory and detoxifying hepatic functions.

CRITERIA

These were suggested by the Paediatric Acute Liver Failure Study Group (PALFSG) and consist of the following:

- Biochemical evidence of acute liver cell injury (usually less than 8 weeks duration)
- No evidence of chronic liver disease
- Coagulopathy—PT >15 seconds or INR >1.5 with encephalopathy not corrected by vitamin K; or PT >20 seconds or INR >2 without encephalopathy

However, previously asymptomatic children with chronic liver diseases such as Wilson's disease, galactosaemia can also present with fulminant hepatic failure for the first time, though they have pre-existing liver disease by definition.

CAUSES

1. Idiopathic—in most cases
2. Infections
   - Viral hepatitis—it occurs due to hepatotropic viruses (hepatitis A, B, C, D, E) and non-hepatotropic viruses (EBV, parvovirus, adenovirus, enterovirus, herpes simplex virus, varicella zoster virus, paramyxovirus). Risk is more when hepatitis B and D coexist. Hepatitis E is more common in adolescents and adults
   - Bacterial infections—enteric fever, Weil's disease (caused by leptospira icterohaemorrhagiae), septicaemia
   - Protozoal infections—falciparum malaria
3. Hepatotoxic drugs—paracetamol overdose, chlorinated hydrocarbons, salicylates, INH, methyldopa, amiodarone, cytotoxic drugs, monoamine oxidase inhibitors, phenytoin, idiosyncratic damage following halothane and sodium valproate
4. Toxins—carbon tetrachloride, amanita phalloides

(mushroom poisoning), methanol
5. Metabolic disorders—Wilson's disease, tyrosinaemia type 1, galactosaemia, hereditary fructose intolerance, neonatal haemochromatosis, Niemann–Pick type C, respiratory chain defects, α-1-antitrypsin deficiency
6. Immunological disorders—autoimmune hepatitis
7. Circulatory causes—ischaemia and hypoxia, hepatic vascular obstruction (Budd–Chiari syndrome), acute circulatory failure, cyanotic heart disease, vascular occlusion, myocarditis, severe asphyxia
8. Miscellaneous—Reye's syndrome, acute leukaemia (leukaemic infiltration), Hodgkin's disease, graft versus host disease, hyperthermia

Viral hepatitis and drug-induced hepatitis are the most important causes of fulminant hepatic failure.

PATHOLOGICAL CHANGES

Liver biopsy shows massive necrosis of hepatocytes which may be patchy or confluent. The reticulin framework of the liver may be collapsed due to multilobular or bridging necrosis. In fulminant hepatic failure, there may be little or no regeneration of hepatocytes. Blood–brain barrier is damaged due to accumulation of toxic products.

The pathological changes depend on the aetiological agents. Some of the specific changes are as follows:

- The hepatocellular necrosis may be diffuse, zonal or centrilobular.
- Centrilobular necrosis is seen in paracetamol poisoning and circulatory shock. Marked cholestasis is seen in the remaining parenchyma.
- Hepatocyte dysfunction rather than injury is seen in Reye's syndrome and tetracycline toxicity.

CLINICAL FEATURES

The children with fulminant hepatic failure may present with or without features of encephalopathy or the features of encephalopathy may be observed at a later stage. In few children the features of encephalopathy may be unrecognised. Such children present only with coagulopathy in the absence of sepsis or DIC. This coagulopathy is not correctable by administration of parenteral vitamin K within 8 hours.

Symptoms

Fulminant hepatic failure may be asymptomatic in children with Wilson's disease. The common symptoms are as follows:

- Jaundice
- Fever, anorexia, vomiting, abdominal pain, foetor hepaticus
- Confusion
- Restlessness
- Deepening jaundice
- Neuropsychiatric changes
- A prodrome of flu-like illness may precede the onset of jaundice
- Irritability, poor feeding and disturbance in sleep pattern in infants

Signs

- Altered consciousness
- Mental changes with 2 weeks of onset of jaundice
- Somnolent
- Poor response to painful stimuli
- Shrinking liver size
- Ascites

COMPLICATIONS

- Infections—bacterial and fungal infections are common
- Hepatic encephalopathy
- Cerebral oedema
- Encephalopathy
- Coagulopathy—GI bleeding
- Renal dysfunction—hepatorenal syndrome
- Hypotension
- Electrolyte disturbances—hypokalaemia, hyponatraemia
- Acid–base imbalance—respiratory alkalosis, metabolic alkalosis, respiratory acidosis
- Pulmonary and cardiovascular problems

INVESTIGATIONS

1. Investigations for ascertaining liver cell injury or failure
   - Serum bilirubin—both direct and indirect are increased.
   - Hepatic enzymes do not correlate with the severity of fulminant hepatic failure. ALT and AST are normal or increased or even decreased. The enzymes are markedly elevated in metabolic disorders. The enzymes are decreased if the liver cell necrosis is severe.
   - Liver biopsy is useful for working diagnosis and subsequent therapy.
2. Investigations for aetiological factors
   - Blood count—white blood cells are increased in infections
   - Serum paracetamol levels
   - Autoantibodies—LKM, ANA and SMA
   - Blood ammonia is elevated in Reye's syndrome
   - Viral markers—hepatitis B (HBV-DNA, antibody to HBV, HBsAg, IgM core antigen [IgM anti-HBcAg]), hepatitis A (IgM anti-HAV), hepatitis C (anti-HCV, HCV-RNA) and hepatitis D (anti-HDV antibody)
   - Urine screening tests for metabolic disorders
   - Succinylacetone is increased in serum and urine in tyrosinaemia
   - Blood urea levels decreased in urea cycle disorders
3. Investigations for complications
   - Prothrombin time is increased
   - Platelet count is decreased
   - Blood sugar is low
   - Aterial blood gas analysis
   - Serum electrolytes—hyponatraemia, hyperkalaemia, respiratory alkalosis and metabolic acidosis
   - Tests for renal function—urea and creatinine are elevated in CRF
   - Coagulation profile—prolongation of prothrombin time (INR) which does not respond to administration of vitamin K

TREATMENT

Supportive

- Maintain normal urine output.
- Correct hypoglycaemia.
- Diet with decreased protein, high calories, high carbohydrates and moderate fat should be given. Total parenteral nutrition may be needed. Special formulas with high branched chain amino acids and low in aromatic amino acids and electrolytes vitamin supplementation should be given.
- Maintain a normal fluid balance. Avoid fluid overload restrict 2 mL/kg/hour. The volume can be monitored by CVP.
- Glucose administration to prevent hypoglycaemia.
- Administration of calcium, phosphorus, magnesium, factor concentrate, magnesium and platelets.
- Gut sterilisation—using antibiotics such as ampicillin/neomycin. Lactulose inhibits colonic organisms.
- Exchange transfusion.
- Coagulopathy can be treated with parenteral vitamin K and plasmapheresis platelet transfusion can be indicated in severe cases. Maintain a platelet count of more than 50,000.
- Liver-assist devices.
- Liver transplantation.
- Flumazenil is a specific benzodiazepine antagonist which binds to the receptor and prevents the binding of benzodiazepine to the receptor.
- L-aspartate and L-ornithine stimulate the hepatic urea cycle activity which utilises the ammonia. Also, they promote glutamine synthesis by the skeletal muscle.

Specific

- Paracetamol poisoning—N-acetylcysteine
- Hepatitis B viral—antiviral agents (lamivudine)
- Autoimmune hepatitis—steroids, azathioprine. Steroids and immunosuppressive drugs may be helpful in autoimmune hepatitis. In other conditions steroids worsen the condition
- Galactosaemia, fructosaemia, hereditary tyrosinaemia type I—dietary elimination

Treatment of Complications

- Treat cerebral oedema
- H2 receptor blockers to prevent GI bleeding
- Avoid nephrotoxic drugs, sedatives, benzodiazepines
- Surgical treatment—orthoptic liver transplantation is the only effective treatment of fulminant hepatic failure
- Indications
- INR >4

PROGNOSIS

The mortality rate is more in children. The mortality varies from 50 to 90% without liver transplantation. The prognosis is poor in infants and young children. This is because of delay in diagnosis as they have an atypical presentation which results in delayed diagnosis. Prognosis depends on the following factors:

- Age of the patient
- Aetiological factors
- Age and onset of encephalopathy
- Serum bilirubin level
- PT level
- Serum creatinine level
- Factor V level
- Arterial pH level

HEPATIC ENCEPHALOPATHY

Hepatic encephalopathy is a complex neuropsychiatric syndrome characterised by disturbances in level of consciousness, behaviour and personality seen in patients with severe acute or chronic liver disease. This fluctuating neurological illness is also associated with asterixis and electroencephalographic changes.

CLASSIFICATION

According to the recommendations by World Congress of Gastroenterology, 1998, hepatic encephalopathy has been categorised into types A, B and C depending on the underlying cause (Table 10.69). Type A (acute) is associated with acute liver cell failure; type B (bypass) is caused by portosystemic shunts without associated intrinsic liver disease and type C (cirrhosis) occurs in patients with cirrhosis. Type C can be episodic, persistent or minimal. Minimal encephalopathy is defined as encephalopathy that does not lead to clinically overt cognitive dysfunction but can be demonstrated with neuropsychological studies.

TABLE 10.69 Types of Hepatic Encephalopathy

Features	Type A	Type B	Type C
Characteristic feature	Acute liver cell failure	Portosystemic shunts (blood bypasses the liver)	Cirrhosis
Underlying condition	Fulminant hepatic failure	Spontaneous or iatrogenic portosystemic shunts	Chronic liver diseases associated with cirrhosis
Prognosis	Poor	Good	Better

PATHOGENESIS

Hepatic encephalopathy occurs either due to diversion of portal blood into systemic circulation through portosystemic collaterals or as a result of hepatic dysfunction. Several different abnormalities contribute to the development of hepatic encephalopathy. Some of these are as follows:

1. Accumulation of neurotoxins in brain—normally, the portal vein carries nitrogen containing waste products from the gut to the liver for detoxification/excretion. In hepatic encephalopathy, this does not occur either because the failing liver cells are not capable of functioning or because the portal blood bypasses the liver through collateral shunts. Ammonia is the most important waste product that accumulates in blood and brain. Other waste products are short chain fatty acids and mercaptans. Ammonia acts in the following ways:
   - Alters the transit of amino acids, water and electrolytes in the astrocytes and neurons.
   - Impairs metabolism of amino acids in the brain.

- Impairs energy utilisation in the brain.
- Inhibits generation of excitatory and inhibitory postsynaptic potentials.
- Direct toxic effect on the neuronal membrane.
- Depress the cerebral blood flow and glucose metabolism.

2. Increased activity of the inhibitory GABA neurotransmission system—GABA is synthesised by the colonic bacteria. It is normally metabolised by liver. In hepatic encephalopathy, it enters the systemic circulation through the portosystemic shunts. In the brain about 24%–45% of the nerve endings are GABAergic. Also, ammonia absorbed by astrocytes leads to swelling of astrocytes. There will be increased activity of inhibitory GABA system which results in decreased energy supply to the brain cells. Increased GABA and benzodiazepines will bind to the GABA-receptor complex which will permit chloride influx into the postsynaptic neuron which will result in generation of inhibitory postsynaptic potential.
3. Imbalance between aromatic and branched amino acids. Aromatic amino acids such as tyrosine, tryptophan and phenylalanine are increased due to poor deamination by the liver. These cross the blood–brain barrier and form false neurotransmitters such as octopamine. There is increased utilisation of branched chain amino acids (valine, isoleucine and leucine) secondary to hyperinsulinaemia due to liver failure.
4. Increase in levels of benzodiazepine-like compounds.
5. Dysregulation of serotonin system.
6. Depletion of zinc and accumulation of manganese.
7. Action of cytokines and bacterial lipopolysaccharide on astrocytes which are formed due to inflammation elsewhere in the body.

CLINICAL FEATURES

The clinical features of hepatic encephalopathy are variable and fluctuating. The symptoms range from mild disturbances of consciousness and altered behaviour to deep coma. Psychiatric changes of varying degree can be seen. These features may be present in association with features of liver failure such as flapping tremor and foetor hepaticus.

In minimal hepatic encephalopathy the children have normal abilities of memory, language, construction and pure motor skills. They have normal standard mental status testing and abnormal psychometric testing. Neuropsychological testing for diagnosis of minimal hepatic encephalopathy includes the block design test, number connecting test and digit–symbol test which are available to test the cognitive functions. Number connecting test is done by measuring the speed at which one could connect randomly dispersed numbers 1–20.

In mild- to moderate-hepatic encephalopathy there is decreased short-term memory or forgetfulness, loss of concentration and irritability. Asterixis, hyperventilation and decreased body temperature can be present. Relative bradycardia may occur in the presence of increased intracranial tension.

Box 10.11 summarises the clinical presentation of hepatic encephalopathy.

CLINICAL GRADING OF SEVERITY

It is done by the West Haven classification system. It is of prognostic significance. The prognosis is better in the Grade I and worse in Grade IV.

West Haven classification

Grade	Criteria
I	Trivial lack of awareness, euphoria or anxiety, shortened attention span, impaired performance of addition or subtraction
II	Lethargy or apathy, minimal disorientation for time or place, subtle personality change, inappropriate behaviour
III	Somnolence to semistupor but responsive to verbal stimuli, confusion, gross disorientation
IV	Coma unresponsive to verbal or noxious stimuli

BOX 10.11 Clinical features of hepatic encephalopathy

	Mental state	Neuromuscular signs
A	Apathy Agitation Altered sleep wake pattern	Asterixis (liver flap or flapping tremors)
B	Behaviour (abnormal—picking at clothes)	Babinski's sign positive (abnormal plantar reflex)
C	Clouding of consciousness Confusion	Cogwheel rigidity
D	Drowsiness Disobedience Delirium Deep coma	Dysarthria Dilated pupils
E	Excessive sleepiness Euphoria	Eye—roving eyes, nystagmus, ophthalmoplegia
F	Fall in mentation	Facies (mask-like)
G	Gross disorientation	Grasp reflex will be present
H	Hypersomnia	Hiccup Hand skills—trouble with writing
I	Inappropriate behaviour Intellectual deterioration	Incoordination Incontinence

DIFFERENTIAL DIAGNOSIS

Hepatic encephalopathy should be differentiated from encephalopathy due to other causes. The following conditions should be ruled out before diagnosis of hepatic encephalopathy is made.

- Organic brain diseases
- Intracranial lesions—intracranial bleeding
- Infections—meningitis, encephalitis
- Metabolic encephalopathy—hypoglycaemia, electrolyte imbalances, hypercarbia, anoxia, uraemia
- Toxic encephalopathy—sedative overdose, hypnotics, antidepressants, antipsychotic agents, salicylates
- Postseizure encephalopathy
- Hyperammonaemia due to urea cycle disorders, following ureterosigmoidostomy
- Alcohol intoxication—resulting in Wernicke's encephalopathy in adolescents and adults

INVESTIGATIONS

The diagnosis of hepatic encephalopathy is mainly clinical and made on the basis of history, physical examination (including mental status) and raised blood ammonia levels.

Confirmation of Liver Disease/ Portosystemic Shunt

1. Liver function tests—show an increase in the following:
   - Serum bilirubin
   - Aspartate aminotransferase
   - Alanine aminotransferase
   - PT (INR) >1.5 with encephalopathy or >2 without encephalopathy
   - Alkaline phosphatase
   - GGT
   - Serum proteins, albumin/globulin ratio
2. Serum ammonia level is increased in most cases with encephalopathy. It is normal only in few cases.
3. Ultrasonogram.

Detection of Causative Factors

- Viral serological markers—HBsAg, HBeAg, anti-HBc, HBV-DNA increased in hepatitis
- TORCH infection screening
- Autoimmune antibodies—antinuclear antibodies (ANA), antismooth muscle antibodies (ASMA), AMA, LKM1 in autoimmune hepatitis
- Serum iron and transferrin for haemochromatosis
- Serum copper, ceruloplasmin, urinary copper for Wilson's disease

- Urine for metabolic disorders
- Sweat chloride and cystic fibrosis mutation studies
- α-1-Antitrypsin levels are decreased in α-1-antitrypsin deficiency
- α-Fetoprotein is a screening test for tyrosinaemia type1
- Serum lactate and pyruvate are increased in glycogen storage disease and respiratory chain defects
- Liver biopsy—cirrhosis

Ruling Other Diseases with Similar Presentation

- CT scan to rule out cerebral haemorrhage—CT scan is normal in hepatic encephalopathy except grade IV hepatic encephalopathy in which cerebral oedema is present.
- Electroencephalography—EEG findings depend on the stage of the encephalopathy. Seizure disorders should be ruled out.
- Cerebrospinal fluid (CSF) analysis to rule out meningitis or encephalitis.
- Blood tests to rule out other causes such as metabolic causes of encephalopathy including hypoglycaemia and uraemia.
- Blood urea and creatinine, electrolytes to rule out renal failure

Detection of Complications

- ABG—hypoxia is common
- Peripheral blood count to rule out infections
- Haemoglobin
- Packed cell volume
- Peripheral smear
- Prothrombin time and activated partial thromboplastin time (aPTT) are prolonged
- Platelet counts are decreased in advanced cases and coagulopathy
- Blood glucose shows hypoglycaemia
- Serum ammonia is elevated
- Urinary electrolytes
- Renal function tests—urea, creatinine and osmolality are elevated in hepatorenal failure

TREATMENT

A patient of hepatic encephalopathy should be treated in an intensive care unit. The conditions that precipitate hepatic encephalopathy should be identified and treated. Appropriate measures to reduce ammonia production should be taken. Offending agents such as high protein diet and drugs should be stopped. Treatment depends on the underlying cause and consists of the following steps.

Steps to Reduce Ammonia

1. Diet—decreased protein intake with high carbohydrates should be given.
   - Calories should be provided by infusion of glucose in the form of 10% dextrose. Maintain a blood sugar above 80 mg%.
   - Protein intake should be restricted to 0.5–1 g/kg/day. If there is malnutrition, adequate proteins should be given to maintain a normal weight. Vegetable proteins are preferred to animal proteins as they are less ammoniagenic and also contain less amounts of methionine and aromatic amino acids. Dietary supplementation of branched chain amino acids is helpful.
   - Fifty per cent of non-protein calories should come from MCT.
2. Lactulose/lactitol for bowel cleaning—lactulose and lactitol are not absorbed in the intestines. They are degraded by the colonic bacteria to lactic and acetic acids resulting in an acidic pH and ammonium ion trapping. They also have a cathartic effect and increase the transit of bowel contents through the gut. They also alter the bacterial flora of the gut. Lactulose is given orally in a dose of 1–2 mL/kg/dose 4 times a day. The total dose is 2.5–10 mL/24 hours. This should produce 2–4 loose acidic stools per day. It may also be administered as an enema in a dose of 40–90 mg/24 hours. Alternatively, phosphate enema can also be given.
3. Bowel sterilisation—neomycin decreases the formation of ammonia and other nitrogenous products by killing the colonic bacteria. Ampicillin can also be given. Rifaximin is a non-

absorbable antibiotic with fewer complications and is used for gut sterilisation.
4. Nasogastric aspiration is done to remove the food and blood in the stomach. This reduces the amount of protein in the gut.
5. High colonic wash.
6. Avoid medications containing ammonia (certain antacids).
7. Plasmapheresis/haemodialysis helps in removal of toxic products and anticoagulants from the circulation.
8. Zinc administration increases ornithine transcarbamylase which is helpful in decreasing ammonia by increasing urea production.
9. L-ornithine and L-aspartate preparation (LOLA) removes ammonia by conversion to urea through the urea cycle. It can be given orally or intravenously. This may be combined with lactulose and rifaximin.
10. Sodium benzoate, 5 g orally twice a day, interacts with glycine to form hippurate which is excreted in urine.

Supportive Care

- Fluid and electrolyte balance should be maintained. Parenteral fluids containing glucose are given to prevent hypoglycaemia. These children are prone to develop hypoglycaemia, as the glycogen reserve in the liver is not available. Fluids should contain about 1 mEq/kg/day of glucose. Metabolic acidosis should be treated with sodium bicarbonate. Metabolic alkalosis should be treated with additional chloride. Potassium chloride is added if hypokalaemia is present.
- Early identification and treatment of GI bleeding, septicaemia and hypoxia.
- Avoidance of precipitating factors—this includes drugs such as thiazide diuretics, morphine, barbiturates, and other sedatives. Paracentesis of large volume of ascitic fluid should also be avoided as it results in electrolyte imbalance which aggravates hepatocellular failure.
- Drugs to improve sensorium—sensorium can be improved by the use of drugs such as flumazenil (benzodiazepine antagonist which may reverse early hepatic encephalopathy), L-dopa and bromocriptine.

Treatment in Resistant Cases

In children who do not improve with treatment, the following supportive measures can be done to improve the quality of life of the child.

- Temporary hepatic support can be done by circulating the blood in another liver.
- Plasmapheresis removes toxic substances present in the blood.
- Exchange transfusion—blood from the child is removed partially and fresh blood from another source is infused.
- Liver assist devices—help to remove toxic substances from the blood.
- Liver transplantation—orthotopic liver transplantation may be lifesaving especially in type A hepatic encephalopathy. Reduced size allografts of liver and living donor transplantation are other options available.

Recent Advances

Some of other modalities tried in resistant cases are as follows:

- Cross-circulation of blood with animals.
- Molecular adsorbent recirculating system (MARS) can be done where albumin bound toxins are removed by dialysis.

Treatment of Complications

1. CNS complications
   - Cerebral oedema—treatment includes elevation of bed by 30°, mannitol infusion, hyperventilation and fluid restriction. Hypothermia and phenobarbitone decrease cerebral metabolism, and thereby cerebral blood flow. This helps in decreasing cerebral oedema.
   - Seizures—phenytoin and gabapentin are safe in hepatic encephalopathy.
   - Cerebral hypoxia—oxygen should be given for hypoxia. N-acetylcysteine infusion increases oxygen delivery and consumption.
2. Hypotension—colloids are indicated to expand intravascular volume in the presence of hypotension. Albumin infusion can also be given.

3. Bleeding—coagulopathy should be treated by parenteral administration of vitamin K (0.2 mg/kg) or fresh frozen plasma. Prophylactic use of ranitidine is beneficial as these patients are prone to develop GI bleeding.
4. Respiratory failure—children with stages III and IV hepatic encephalopathies are prone to develop airway obstruction and respiratory arrest due to decreased protective gag reflex. Such patients should be intubated and given assisted ventilation. Endotracheal intubation may be useful in preventing aspiration also.
5. Renal failure—if hypovolaemia is present and CVP is low, fluids should be given. Pre-renal failure should be treated with adequate intravenous fluids. Furosemide in a dose of 1–2 mg/kg can be given intravenously in early stages of renal failure if the CVP is more than 8–10 cm of water. Haemodialysis is done in established cases of renal failure (persistent oliguria <1 mL/kg/hour). Urine output should be maintained. Dopamine can be given to improve renal perfusion.
6. Ascites—can be treated with 5% albumin infusion. Bile acid binders can be given to prevent accumulation of bile acid

MONITORING

The child has variable presentation and the clinical features are fluctuating from time to time. Hence, it is necessary to monitor various parameters during treatment and follow-up so that early identification of complications and intervention can be done. Monitoring protocol in a case of hepatic encephalopathy is given in Table 10.70.

TABLE 10.70 Monitoring Protocol of a Child with Hepatic Encephalopathy

Daily	Once in 3 Days	Weekly
Blood glucose (2 hourly) Serum electrolytes—sodium, HCO_3 K^+ Haemoglobin Packed cell volume Peripheral smear	Renal function tests (urea, creatinine) Prothrombin time NEC (blood non-enteric culture)	Serum amino acids EEG

Clinical Parameters

The clinical improvement should be monitored frequently to assess the efficacy of treatment.

- Neurological grading—level of consciousness
- Daily weight
- Vital signs
- CVP
- Liver span
- Abdominal girth for monitoring the progression/regression of ascites
- Intake/output chart

Laboratory Parameters

- ABG—hypoxia is common
- Peripheral blood counts to rule out infections
- Platelet counts are decreased in advanced cases and coagulopathy
- Urinary electrolytes
- Renal function tests—urea and creatinine are elevated in hepatorenal failure
- Urine osmolality
- Prothrombin time is prolonged
- Serum amino acids are decreased
- Serum ammonia is elevated
- Liver function tests

Infection Surveillance

Infections are more common in children with liver cell failure. Infections should be suspected and treated early. The prognosis is poor in the presence of the following infections:

- Blood counts
- ESR
- Acute phase reactants—C-reactive protein (CRP)
- Chest radiograph
- Cultures—blood non-enteric culture (NEC), urine, throat, sputum

PROGNOSIS

Prognosis of hepatic encephalopathy depends on various factors such as age, duration, coma grade, complications and response to treatment. For instance, the prognosis is better for encephalopathy of acute

TABLE 10.71 Prognostic Indicators in Hepatic Encephalopathy

Features	Good Prognosis	Poor Prognosis
Age	Children	Adolescents and adults
Aetiology	Paracetamol poisoning Hepatitis A	Hepatitis C
Duration of encephalopathy	<7 days	>7 days
Coma grade	I and II	III and IV
Liver size	Enlarged	Shrinking or non-palpable liver
Bleeding tendency	Absent	Present
Fluid retention	Absent	Present
Serum albumin	Normal	Decreased
Serum bilirubin	Normal	Increased
Prothrombin time	Normal	Prolonged
Liver enzymes—AST, ALT	Normal	Increased
α-Fetoprotein secreted during treatment by the regenerating cells	Increased	Decreased
Complications	Not present	Increased intracranial tension Respiratory failure Convulsion Renal failure Haemorrhage Sepsis
Improvement of sensorium with treatment	Rapid improvement in sensorium	No improvement in sensorium after 48 hours of treatment

onset as compared to that of chronic form. The prognosis is poor in patients progressing to coma. These factors are summarised in Table 10.71.

WILSON'S DISEASE

Wilson's disease, also known as hepatolenticular degeneration, is an autosomal recessive genetic disorder. It is characterised by the inability of the liver to transport and store the normally absorbed dietary copper. This results in an abnormal deposition of copper in the liver, basal ganglia, eyes and other tissues.

GENETICS

The abnormal gene is located in the long arm of chromosome 13 (13q14.3). In its normal state, this gene (ATP7B) encodes a copper transporting P-type ATPase, which plays an active role in biliary copper excretion and incorporation of copper into ceruloplasmin. The incidence of this autosomal recessive genetic condition in the homozygous form is one in 40,000 to 1 in a lakh.

PATHOGENESIS

In this condition, serum ceruloplasmin (copper-transporting protein) is either decreased or absent. This results in defective copper excretion into the bile and leads to accumulation of copper in the cytosol of hepatocytes (liver cells). Once the liver cells are overloaded with copper, the copper deposition occurs in the other tissues (Fig. 10.28).

Copper is an inhibitor of certain enzymatic processes. Ionic copper inhibits pyruvate oxidase in brain and decreases ATP in cell membranes. The ATP-phosphocreatine and potassium content of the tissues are also decreased. The periportal hepatocytes are infiltrated with lymphocytes and plasma cells. There is piecemeal necrosis, bridging necrosis, fibrosis, micronodular cirrhosis and fulminant hepatitis. Liver cell damage by the free radicals produced by copper and similar degenerative changes in the lenticular nuclei of brain can be seen.

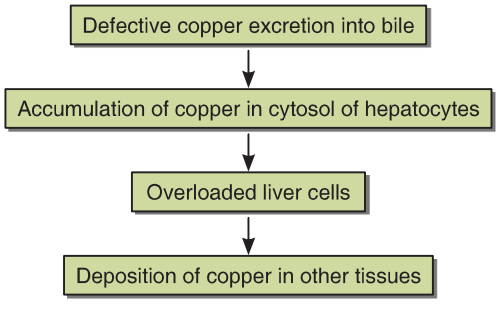


FIGURE 10.28 Pathogenesis of Wilson's disease.

CLINICAL FEATURES

Copper first gets accumulated in the liver; hence, the usual presentation during childhood is that of hepatic disease. After the liver gets saturated, copper gets accumulated in the nervous system, cornea, kidneys and other organs. The fulminant presentation of the disease is more frequent in females.

Modes of Presentation

There is a great deal of variability in the clinical presentation. It depends on the organ of primary involvement. Most patients present in the first to second decade of life with hepatic manifestations. Some patients present during the third or fourth decade with primarily neurologic or psychiatric manifestations. The common modes of presentation are discussed further.

Hepatic Manifestations

Hepatic involvement is the predominant manifestation. The clinical features due to liver involvement include

- Asymptomatic hepatomegaly
- Hepatitis—subacute or chronic active hepatitis, or chronic hepatitis
- Cirrhosis of liver
- Fulminant hepatic failure
- Cryptogenic cirrhosis

Haemolytic Form

Haemolytic anaemia may be an initial manifestation, possibly related to the release of large amounts of copper from the damaged hepatocytes. This form of Wilson's disease is usually fatal without transplantation. During the haemolytic episodes, urinary copper excretion and serum copper levels (non-ceruloplasmin-bound) are extraordinarily elevated.

CNS Manifestations

Neurologic symptoms predominate the neuropsychiatric disorders and may develop insidiously or precipitously, with intention tremors, dysarthria, dystonia, deterioration in school performance or behavioural changes.

Neurological Manifestations

- Tremors (resting tremor, intention tremor)
- Chorea
- Dystonia
- Dysphagia
- Speech abnormalities (dysarthria)
- Difficulty in writing
- Drooling of saliva
- Dementia
- Deterioration in school performance
- Change in handwriting

Psychiatric Manifestation

- Maniac-depressive psychosis
- Mood/behaviour changes
- Bizarre behaviours

Ophthalmologic Manifestations

Clinical features due to involvement of eyes include

- Kayser-Fleischer ring
- Sun-flower cataract

Kayser–Fleischer Ring. It is a golden-brown or greyish-brown ring at the limbus or at the periphery of the cornea. The ring is better seen superiorly and inferiorly than laterally and medially. It may be unilateral or bilateral and complete or incomplete.

It is seen in 98% of neurologically symptomatic and 40% of asymptomatic patients with Wilson's disease. Although it is a pathognomonic sign of Wilson's disease, it may be absent in young patients with hepatic symptoms. It may also be seen in some familial cholestatic syndromes and chronic active hepatitis with cirrhosis.

The ring may be visualised by the naked eye on torch light examination or with simple magnification or slit-lamp examination. On slit-lamp examination, the ring appears as a golden-brown to green deposit at the level of the Descemet's membrane in peripheral cornea. It is usually bilateral and ranges from 1 to 3 mm in width. The pigmentary deposits are more prominent at the 12 and 6 o'clock positions.

When observed over a period of time, the deposition begins in the superior cornea, then proceeds to the inferior cornea and eventually forms a complete ring. After a complete ring is formed it

progresses centrally. Treatment with D-penicillamine causes the ring to disappear, in the reverse order of its formation.

Significance of KF ring—it indicates the release of hepatic copper into the circulation and its subsequent deposition in the brain. Formation of KF ring is usually accompanied by neurologic and psychiatric manifestations. It does not cause any visual disturbances.

Renal Manifestations

Manifestations of progressive renal failure with alterations in tubular transport of amino acids, glucose, galactose, pentose, uric acid, phosphate and calcium may be present.

- Urolithiasis
- Haematuria
- Proteinuria
- Nephrocalcinosis

Skeletal Manifestations

- Osteoarthritis
- Osteochondritis
- Osteomalacia

Other Manifestations

- Pancreatitis
- Cardiomyopathy
- Cardiac arrhythmias
- Amenorrhoea and spontaneous abortions in adolescent and adult females

Asymptomatic

Few cases do not have any symptoms, but investigations show findings of Wilson's disease.

INVESTIGATIONS

1. Serum ceruloplasmin level is less than 20 mg/dL (normal: 27–37 mg/dL).
2. Serum free copper level (non-ceruloplasmin bound copper) is increased. As the free copper cannot be measured directly, the total serum copper and ceruloplasmin are measured and the free copper is estimated (0.047 mmol of copper is bound to 1 mg of ceruloplasmin).

$$\text{Free copper} = \text{total serum copper} - \text{amount of copper bound to ceruloplasmin}$$

3. Twenty-four-hour urinary copper excretion
   - Normal value is <40 μg in 24 hours (usually 0–25 μg/day).
   - It is increased to >100 μg/day in patients with Wilson's disease.
   - In doubtful cases, copper excretion in urine after chelation by 1 g of D-penicillamine given orally in two divided doses helps in the diagnosis. Excretion of copper in the urine is 1200–2000 μg/day in Wilson's disease.
4. Slightly abnormal liver function tests such as a raised aspartate transaminase, alanine transaminase and bilirubin level.
5. Liver biopsy
   - Liver copper level is increased to more than 250 μg/g of dry weight of liver in patients with Wilson's disease. Normal liver copper level is less than 10 μg/g of dry weight of liver.
   - Copper stains on liver biopsy are positive in patients with Wilson's disease. Other features such as microvesicular fatty infiltration of hepatocytes, hepatocellular necrosis and macronodular cirrhosis can also be seen.
6. Radioactive copper loading test—in this test radioactive copper (Cu_{64}) with an activity of 0.5–2 mCi is given orally to the child after fasting for 8 hours. Measure the serum radioactivity at 1, 2, 4, 24 and 48 hours after the intake. In normal subjects, the radioactive copper level rises in the serum within 1–2 hours and then disappears in 4–6 hours followed by a secondary rise at 24–48 hours. This is because the liver synthesises ceruloplasmin and the copper gets incorporated into it (resulting in disappearance from serum) and released into the circulation (resulting in secondary rise). In Wilson's disease as the ceruloplasmin levels are decreased, this secondary rise is absent.
7. Coomb's negative haemolytic anaemia.
8. Molecular diagnosis by DNA mutation analysis or linkage analysis.

These are summarised in Table 10.72

TABLE 10.72 Investigations in Wilson's Disease

Investigation	Normal	Wilson's Disease	Inference
Serum total copper level	80–190 µg/dL	< 20 µg/dL	Low
Serum free copper	<1.6 µmol/L	>7 µmol/L	Free copper is increased
Serum ceruloplasmin	27–37 mg/dL	<20 mg/dL	Decreased
24-hour urinary copper excretion	Usually <40 µg/day	>100 µg/day	Increased
Liver copper µg/g dry weight	<10	>250	Increased
Urine copper µmol/24 hour	<1.25	>3	Increased
Urine copper µmol/24 hour after penicillamine	<25	>25	Increased

DIAGNOSTIC CRITERIA

Minimum Diagnostic Criteria

- Clinical presentation, usually in the form of hepatic involvement or extrapyramidal neurologic involvement.
- Kayser–Fleischer rings in the cornea (confirmed by slit-lamp examination).
- Twenty-four-hour urine copper excretion greater than 100 µg.

Ancillary Diagnostic Criteria

The presence of any of the following two is diagnostic of Wilson's disease:

1. Serum ceruloplasmin level decreased
2. Urinary copper: >100 µg/day and up to 1000 µg/day
3. Liver biopsy: >250 µg/g dry weight

TREATMENT

The aim of treatment is to maintain serum copper levels within normal limits. Early initiation of treatment with chelating agents carries good prognosis. Continuous lifelong treatment is required.

Diet Modification

- A diet with high protein and low copper should be given.
- It is advisable to adopt a low copper diet with the copper intake restricted to less than 1 mg/day.
- The food products rich in copper include ground nuts, chocolate, mushrooms, unprocessed wheat, liver, dried fish, dried beans, green chillies, shell fish, legumes should be avoided.
- Cooking food in copper vessels should be avoided.

Drug Therapy

Copper Chelating Agents

1. D-Penicillamine—it combines with copper to form relatively non-toxic, water-soluble complexes which can be excreted. Depending on the urinary copper levels, the dose can be adjusted. Continued administration for at least 2 years improves liver and neurological function and disappearance of KF rings. Lifelong therapy is needed with oral penicillamine. A dose of 20–25 mg/kg/day in two divided doses for children under 10 years and 1 g/day for children above 10 years should be given. It should be given before meals. Penicillamine is an antimetabolite of B_6. It causes pyridoxine deficiency, so pyridoxine supplementation (25 mg/day) will be beneficial in children treated with penicillamine.
2. Trientine dihydrochloride (triethylene tetramine dihydrochloride [TETA]) can be used in children who do not tolerate penicillamine. It is given in a dose of 20 mg/kg/day in three divided doses up to a maximum of 400–800 mg/day. It can be given 1 hour before food or 2 hours after food. It is less toxic than penicillamine and is more useful in children with neurological manifestations.

Metal-Containing Drugs

The following two metal-containing drugs prevent the absorption of copper from the gut.

- Zinc—elemental zinc given as zinc acetate inhibits GI absorption of copper. It induces metallothionein synthesis in the absorptive cells of the gut.

Copper binds to the metallothionein and is shed off in the lumen along with these cells. A dose of 100–150 mg/kg/day is given in three divided doses. The dose can be increased to 300 mg/day.

- Molybdenum ammonium tetrathiomolybdate blocks the absorption of copper by forming copper complexes in the gut which are excreted in stools. A dose of 30 mg is given twice daily.

Liver Transplantation

Liver transplantation is considered a therapeutic option in the following cases with Wilson's disease:

- Fulminant hepatic failure or irreversible liver damage
- No response to treatment

Antioxidant Therapy

Cuprous ions result in oxidative damage to the hepatocytes and mitochondria. Hence, an antioxidant, like α-tocopherol may be useful in Wilson's disease. It is given in a dose of 10–15 mg/day.

Recent Advances

Gene therapy is the new modality of treatment. Normal allele of the Wilson gene can be introduced into the patient who is homozygous. More efficient methods for gene delivery to all hepatocytes in the liver are under trial.

MONITORING OF THE CHILD UNDER TREATMENT

The child should be monitored for development of complications such as cirrhosis. Liver biopsy should be done every 3–5 years. Urine copper is not a good guide and hence not useful in monitoring the child with Wilson's disease.

PROGNOSIS

The prognosis of the condition depends on the initiation of the treatment and the response of the patient. If there is response to penicillamine by 6 months, the prognosis is good. In fact, in asymptomatic patients, the expression of this disease can be prevented by early initiation of therapy. Kayser–Fleischer ring disappears in 3–5 years of treatment with chelating agents.

Poor prognosis is seen in the following conditions:

- Dystonia
- Chronic active hepatitis
- Acute neurological form associated with irreversible cystic changes in the basal ganglia

If the condition is not treated in time, it may result in death. The causes of death in Wilson's disease include:

- Liver cell failure
- GI bleeds
- Recurrent infections
- Hepatic, neurologic, renal and haematological complications

GENETIC COUNSELLING

Wilson's disease can occur in other family members. This is an autosomal recessive disorder. If one parent is a carrier there is no chance of the children having the disease. Twenty-five per cent of the children will be carriers. If both the parents are carriers, 25% of the children will have the disease, 50% will be carriers and 25% will be normal (Table 10.73).

Screening is done by an ophthalmic examination for KF rings and 24-hour urine copper excretion. Family members of proven cases should be screened by determining the serum ceruloplasmin levels and urinary copper excretion. If the results are abnormal, liver biopsy should be done to confirm the diagnosis.

TABLE 10.73 Risk for Wilson's Disease in the Family

Persons at Risk	Risk
Parents	Parents will be obligate heterozygotes
Risk to the siblings of a proband	25% will have the disease 50% will be unaffected carriers 25% will be normal
Risk to the offsprings of a proband	The offsprings of an affected person will be obligate carriers

CHAPTER 11

Disorders of Central Nervous System

HISTORY TAKING

Name

It gives a clue about the religion the child belongs to. Eating habits vary with religion. Neurocysticercosis is common in Hindus who eat pork unlike Muslims who do not eat pork.

Age

- Simple febrile fits are common in the age group of 6 months to 5 years.
- Thromboembolism is common in young age group.
- Cerebral haemorrhage is more common in adults.

Sex

- Adrenoleukodystrophy is an X-linked recessive disorder common in boys.

Place

- Encephalitis is common in places where pigs are reared.
- Lead encephalopathy is common in areas with automobile or pencil factories.

Informant

The developmental milestones told by the mother are always more reliable as compared to any other person, including father. Hence, the history should be sought from the mother in most cases, if possible. In few children who are reared by grandparents, history should also be sought from them.

Reliability

If the informant is not reliable, more emphasis should be given to the clinical examination. Most of the mothers are not ready to accept the fact that something is wrong with their child if the child is mentally retarded. Hence, history should be elicited carefully.

Presenting Complaints

- Altered sensorium
- Inability to use the limbs, paucity of movements, etc.

History of Presenting Illness

Onset

- Acute onset—seen in head injury and acute infections (meningitis and encephalitis)

- Subacute onset—infections with low virulence
- Chronic onset—neoplastic disorders, degenerative disorders, demyelinating disorders
- Paroxysmal—epilepsy, migraine, multiple sclerosis, hysterical, periodic paralysis

Precipitating Factors

This history is usually elicited by asking the following questions:

- When did it start? (time of the day)
- What was the child doing when it started? (while working, during sleep or immediately after waking up) (Table 11.1)

Course of Illness

- Progressive/static/improving (Table 11.2).
- Progression of paralysis over hours to days—stroke in evolution.
- Total paralysis—complete paralysis seen from onset or within 1 or 2 hours (cerebral haemorrhage).
- Paralysis increases in a step-wise manner (stuttering paralysis).
- Was the severity maximal at the onset?
- Is the neurological impairment ascending (starts in the legs and ascends towards the head) or descending (starts in the head and descends towards the legs)?
- Meningococcal meningitis progresses rapidly.
- Tuberculous meningitis (TBM) runs a chronic course.

TABLE 11.1 Precipitating Factors of CNS Diseases

Precipitating Factors	Conditions
During sleep or immediately after waking up	Cerebral thrombosis
Exertion activity	Embolism
Strain or stress	Haemorrhage
Following generalised convulsions	Todd's palsy

TABLE 11.2 Progression of Weakness and Associated Aetiological Factors

Progression	Aetiological Factors
Improves with time	Thromboembolic manifestations
Static	Cerebral palsy
Deterioration	Degenerative disorders, tumours

- Duration of paralysis—few minutes to hours/recovers within 24 hours from the onset (transient ischaemic attacks)/lasts for hours to days/persists (cerebral palsy).

Associated Complaints

- Fever—low grade/high grade, continuous/intermittent, associated with chills and rigours.
- Convulsions—this is often the presenting complaint. The attendant should be asked to describe the seizure in detail under the following heads: focal/generalised/secondary generalisation, associated factors (aura, loss of consciousness, bowel/bladder incontinence, frothing from mouth, uprolling of eye balls, etc.), postseizure weakness, precipitating factors (dehydration, stress, fever), association with time of day, past episodes, family history, drug intake. In children between 6 months and 5 years, one of the common causes of convulsions is febrile seizures, which can be typical or atypical. A typical febrile seizure lasts for less than 15 minutes and is usually seen within the first 24 hours of onset of fever. It is always generalised; there is familial predisposition and there are no focal neurological deficits.

History Related to Higher Functions

- Level of consciousness—recognises mother/father/others, loss of consciousness, duration of unconsciousness, whether recovered/deteriorating
- Orientation—to time, place and person
- Behaviour—H/o change in behaviour. Note whether the child is interested in surroundings, playing well, eating well, associating well and sleeping well
- Cognitive functions—speech and language, loss of memory (both recent and remote memory), intelligence (changes in school performance)
- Emotional disturbances—H/o excessive laugh or cry, incoherent talks, violent behaviour, picking at clothes

History Related to Sleep

- Sleep pattern normal or distorted
- H/o insomnia/excessive sleepiness

History of Handedness

Early hand preference before 12 months is seen in hemiplegia.

History Related to Cranial Nerve Involvement

- H/o abnormal smell
- H/o blurring of vision
- H/o squint
- H/o drooling of saliva
- H/o collection of food in the cheeks
- H/o deviation of angle of mouth while eating
- H/o tinnitus
- H/o vertigo
- H/o nasal regurgitation
- H/o change of voice (hoarse voice, nasal twang in voice)

History Related to Motor System

- Nutrition—H/o wasting/thinning of muscles
- Tone—H/o child being stiff or flaccid (Box 11.1)
- Power—H/o weakness (proximal/distal) (Table 11.3)
- Coordination—H/o spillage of water while taking near the mouth

History Related to Stance and Gait

- Stance—whether sways while standing
- Gait—whether able to walk normally or not

History of Involuntary Movements

- Type of involuntary movements—slow (athetosis, dystonia)/fast (chorea, ballismus)

BOX 11.1 History to be noted for alterations in tone

Increased tone	Decreased tone
H/o stiffness H/o difficulty in wearing napkins, toilet care H/o holding the child on the hip H/o toe walking H/o tendency for scissoring (adductor spasm)	H/o flaccidity H/o floppiness H/o slipping between mother's hands H/o increased range of movements in the joints

TABLE 11.3 History to be Noted for Alterations in Power

Weakness	History
Upper limbs	
Proximal	H/o difficulty in lifting the arm above the head H/o difficulty in combing the hair H/o difficulty in taking objects from a height
Distal	H/o difficulty in writing H/o difficulty in mixing food H/o difficulty in buttoning H/o difficulty in dressing/undressing H/o difficulty in eating with a spoon
Neck	Can the child lift the head from the bed?
Trunk	Can the child turn in the bed? Can the child get up from supine position?
Lower limbs	
Proximal	H/o difficulty in getting up from sitting position, supine position H/o difficulty in climbing up and down the stairs
Distal	H/o difficulty in holding the chappals without slipping (while walking) H/o difficulty in walking with chappals held in the foot H/o dragging of foot while walking H/o tripping of toes while walking

- H/o fasciculations
- When exaggerated/absent—chorea is exaggerated by stress and absent during sleep

History Related to Sensory System

1. H/o root pain
2. H/o altered sensations—hypaesthesia/hyperaesthesia, positive symptoms (pins and needle sensation, tingling sensation), negative symptoms (numbness)
3. Cortical sensations
4. Lateral column sensations—crude touch, pain and temperature
   - Is the child able to appreciate touch?
   - Is the child able to appreciate clothes on the body?
   - Is the child able to appreciate warmth while taking bath with warm water?
   - Is the child able to appreciate cold temperature?
   - Is the child able to appreciate the pain of injections/insect bites?

5. History related to posterior column sensations (joint position, vibration)
   - H/o altered sensation while walking such as walking on a cotton wool
   - H/o falling while washing (washbasin symptom—as the child closes the eyes the position sense is lost)
   - Is the child able to appreciate the position of joints?

History Related to Cerebellar Symptoms

- H/o flailness (hypotonia)
- H/o ataxia
- H/o titubation (nodding movement of head)
- H/o nystagmus
- H/o staccato speech
- H/o intention tremor
- H/o change in handwriting (macrographia)
- H/o ataxic gait
- H/o inability to perform alternating movements
- H/o swaying or tendency to fall on standing or walking

History Related to Autonomic System

- H/o bladder and bowel disturbances
- H/o vasomotor changes in skin—flushing of skin, sweating (absent/excessive), pallor, coldness, piloerection, oedema
- H/o giddiness while getting up from sitting position (postural hypotension)
- H/o palpitation
- H/o salivary disturbances—scant, thick viscid saliva or copious thin watery secretions
- H/o wheezing (bronchoconstriction)
- H/o problems of erection of penis (in adolescents and adults)

History Related to Spine and Cranium

- H/o pain in the back
- H/o spinal deformities
- H/o painful spinal movements
- H/o increase or decrease in head size

History Related to Complications

- H/o bedsores
- H/o contractures

Symptoms of Increased Intracranial Tension

- H/o headache
- H/o vomiting
- H/o visual disturbances—blurring of vision (due to papilloedema), photophobia
- H/o convulsions/coma

Aetiological History

- H/o diarrhoea/dehydration
- H/o visual disturbances (triad of symptoms in carotid hemiplegia—ipsilateral monoocular blindness, contralateral facial weakness and hemiplegia)
- H/o trauma—intraoral injury, head injury
- History related to infections—ear discharge, sore throat, exanthematous fevers, fever with chills and rigours (infective endocarditis, malaria)
- H/o fever, headache, altered sensorium (CNS infection)
- History related to cerebral palsy—permanent clenched fist, delay in sitting/crawling/walking, inability to feed self, etc.
- History related to meningeal irritation—painful movements of the neck
- History related to soft neurological signs (for details, see section *Soft Neurological Science and Symptoms*, page 575)—difficulty in jumping after 3 years of age, difficulty in hopping after 5 years of age

History Related to Other Systems

1. Cardiovascular system
   - H/o palpitations
   - H/o cyanosis
   - H/o headache (hypertension)
   - H/o fever (infective endocarditis)
2. Respiratory system
   - H/o cough of chronic duration (tuberculosis is associated with TBM, tuberculoma, tuberculous endarteritis, etc.)
   - H/o foul smelling sputum (suppurative lung diseases predispose to infections spreading to brain)
   - H/o orthopnoea (in bilateral diaphragmatic palsy)

- H/o abnormal breathing (pontine, brainstem lesions)
- H/o paradoxical breathing is seen in diaphragmatic paralysis
- H/o Cheyne–Stokes breathing is seen in increased intracranial tension

3. Gastrointestinal system
   - H/o diarrhoea
   - H/o dysentery—shigella encephalopathy (associated with haemolytic uraemic syndrome)
   - H/o vomiting (increased intracranial tension, space occupying lesions)
4. Haematological system
   - H/o bleeding (idiopathic thrombocytopenic purpura, bleeding disorders)
   - H/o bleeding gums, bony tenderness (leukaemia)
   - H/o pain in the fingers, hand, foot, abdomen (sickle cell anaemia)
   - H/o dysentery (haemolytic uraemic syndrome)
5. Musculoskeletal system
   - H/o wasting of muscles seen in upper motor neuron (UMN) and lower motor neuron (LMN) lesions

History of Past Illness

- H/o similar illness in the past
- H/o transient ischaemic attacks
- H/o convulsions
- H/o head injury
- H/o ear infections (predisposes to brain abscess)
- H/o rheumatic fever (predisposes to embolism)
- H/o hypertension (cerebral haemorrhage, transient ischaemic attacks)
- H/o cardiovascular disorders—breathlessness, cyanosis, chest pain, syncopal attacks. Congenital heart disorders predispose to embolism due to atrial fibrillation, subacute bacterial endocarditis, reversal of shunt resulting in paradoxical embolism. Cyanotic heart disorders predispose to cerebral infarction or abscess.

Treatment History

- H/o repeated blood transfusions (haemolytic anaemia—sickle cell crisis)
- H/o surgery
- H/o cranial irradiation

History of Contact

- H/o contact with a case of tuberculosis predisposes to CNS tuberculosis, meningitis and tuberculoma.

Antenatal History

- H/o fever with rash or painful lymphadenopathy (intrauterine infections)
- H/o decreased movements in utero (motor neuron disease)
- H/o prolonged duration of labour (predisposes to asphyxia)

Birth History

- Nature of delivery—vaginal or caesarean
- H/o forceps delivery
- H/o birth asphyxia
- H/o preterm (prone for intraventricular haemorrhage)
- H/o birth injury

Neonatal History

- H/o fever, rash, petechial haemorrhages, jaundice, cataract (markers of intrauterine infections)
- H/o umbilical cord catheterisation/sepsis (predisposes to embolism)
- H/o cyanosis, breathlessness at birth (cardiac disorders predispose to embolism)
- H/o jaundice (prone for kernicterus, cerebral palsy)
- H/o neonatal convulsions (intrauterine infections)
- H/o poor feeding
- H/o lethargy
- H/o umbilical catheterisation (prone to infection and embolism)

Developmental History

- H/o delayed milestones
- H/o delay in sitting, crawling and walking
- H/o standing with support at an early age than expected is seen due to spasticity of lower limbs in spastic cerebral palsy

Nutritional History

- H/o nutritional disorders—thiamine deficiency results in dry beriberi that presents with neurological manifestations.

Immunisation History

- H/o recent vaccination
- H/o convulsions is seen after immunisation with DPT
- H/o vaccine induced mumps, rubella
- H/o antirabies vaccine

Personal History

- H/o sedentary habits
- H/o sports activity, use of motor vehicle or any other activity of child predisposing to accidents
- H/o smoking—in adolescents and adults
- H/o alcohol—in adolescents and adults
- H/o drug abuse—such as intravenous drugs predisposing to infection or thromboembolism in adolescents and adults

Family History

- H/o convulsions
- H/o neurological disorders, degenerative disorders (spinocerebellar degeneration)
- H/o metabolic disorders
- H/o diabetes
- H/o hypertension
- H/o migraine

Social and Environmental History

- Viral encephalitis is common in the areas where pigs are reared.
- Lead encephalopathy and neuropathy are common in areas where factories related to automobiles and pencil manufacturing are located.

GENERAL EXAMINATION

Many neurological disorders are associated with skin lesions such as café au lait spots, adenoma sebaceum and telangiectasia. These are known as neurocutaneous markers and are seen in association with neurological diseases because both skin and nervous system develop from the ectoderm. A thorough general examination is always helpful in diagnosis.

General Appearance

The general appearance of the child (healthy, unwell or ill) can reveal valuable information that can help in diagnosing the underlying CNS disorder.

Consciousness and Mental State

Consciousness is the state of awareness of one's own self and the environment. It can be altered in various conditions such as meningitis and metabolic disturbances. A disturbed level of consciousness may vary from a mild confusional state to even coma. The altered levels of consciousness and the Glasgow Coma Scale have already been discussed in detail in Chapter 3.

Nutritional Status

It should be noted whether the child is well nourished or undernourished. A child suffering from TBM may be undernourished, while the one suffering from stroke is usually obese.

Growth Problems

- Generalised growth retardation—in bilateral cortical lesions (quadriplegic cerebral palsy) and chronic neurological disorders
- Localised growth retardation—in infantile hemiplegia growth of the body on one side is affected (length of the limbs decreased, finger and nail size small)
- Tall/short
- Obese/thin

Posture

The posture or attitude constantly assumed by the

child while at rest or in motion should be noted. Certain abnormal posturing is seen in lesions of the CNS. Consistently maintained asymmetric posture (such as bedridden, ambulatory/motionless, opisthotonus, inability to rise when asked to) should be evaluated. Posture while lying down, standing and sitting should also be noticed (see also Chapter 3)

Vital Signs

The vital signs are controlled by the centres in the CNS and depend on feedback received through the peripheral nervous system. Hence any lesion in the nervous system can affect the vital signs.

- Pulse—feel for all peripheral pulses. They may be absent in thromboembolism (stroke). Bradycardia is seen in children with increased intracranial tension (Cushing's triad—bradycardia, hypertension and altered respiration). Irregular pulse is seen due to reflex dysautonomia in spinal transection above T_6.
- Respiratory rate—central hyperventilation.
- Blood pressure—elevated in children with increased intracranial tension. Hypertension is associated with cerebral haemorrhage, subarachnoid haemorrhage and thrombosis.
- Temperature—increased in CNS infections. Hyperpyrexia occurs in pontine haemorrhage.

Anthropometry

In long-standing nervous system disorders, the affected part shows wasting or growth retardation. Hence measuring the body parts is helpful to arrive at a diagnosis.

The significant anthropometry findings include

- Weight—obesity is associated with thrombosis
- Height/length—length should be measured in a child who is bedridden. It is decreased in infantile hemiplegia of long duration
- Midarm circumference—decreased in muscle wasting
- Head circumference—decreased in microcephaly, increased in hydrocephalus, megalencephaly and intracranial space-occupying lesions (cerebral tumours).

Head-to-Toe Examination

1. Head—abnormal shape and size should be checked. In basilar invagination, head appears to lie in extension on a short neck, with low hairline and limited neck movements
2. Eyes—findings present in eyes may give clue about the associated CNS conditions such as:
   - Telangiectasia in the bulbar conjunctive may be associated with telengiectasia in the brain (ataxia telangiectasia). Subconjunctival haemorrhage may also be associated with intracranial haemorrhage
   - Jaundice is associated with hepatic encephalopathy
   - Phlycten is seen in children with tuberculosis (TBM)
   - Drooping of eyelids (myasthenia gravis)
   - Fixed unilateral droop (third cranial nerve palsy)
   - Unilateral ptosis with enophthalmos and small pupil (Horner's syndrome)
   - Flickering around eyes, clonic spasm of orbicularis oculis and oris (myokymia)
   - Eyes turn up without the lid closing (LMN facial palsy)
3. Face—dysmorphic facies are seen in chromosomal abnormalities and may be associated with mental retardation (Table 11.4)
4. Neck
   - Extreme tenderness at the sides of the neck is seen in lateral sinus thrombosis
   - Torticollis or wry neck (*torti*—twisted, *collis*—neck) is seen in lateral rectus palsy, quinsy, posterior fossa or cerebellar tumours
   - Neck stiffness occurs in meningeal irritation
   - Lymphadenopathy is associated with tuberculosis (TBM), anticonvulsant therapy with phenytoin (secondaries in brain due to leukaemia, cerebral haemorrhage)
5. Limbs
   - Koilonychia—seen in iron deficiency anaemia which is associated with decreased attention span, alertness and learning
   - Oedema—seen in hepatic failure which may present as encephalopathy

TABLE 11.4 Dysmorphic Facies and Associated Nervous System Disorders

Condition	Dysmorphic Features	Nervous System Features
Hypothyroidism	Coarse facies	Mental retardation
Down's syndrome	Mongoloid facies	Low IQ
Moebius syndrome	Mask-like facies	Bilateral VI and VII nerve palsy
Prader–Willi syndrome	Almond-shaped palpebral fissures, fish-like mouth	Mental retardation
Wallenberg syndrome	Telecanthus	Sensorineural deafness
William's syndrome	Elfin facies	Mental retardation
Coffin–Lowry syndrome	Coarse facies	Severe mental retardation
Sotos syndrome	Coarse looking facies with large dolichocephalic head	Mental retardation
Fragile X syndrome	Long facies	Autistic or aggressive behaviour

- Peripheral nerve thickening—seen in hereditary neuropathy

6. Skin
   - Pallor—seen in vasomotor collapse/anaemia (intracranial haemorrhage)
   - Icterus (kernicterus in newborn, liver failure with hepatic encephalopathy)
   - Neurocutaneous markers—café au lait spots, adenoma sebaceum, etc. (Table 11.5; see also Figs. 11.1–11.3)
   - Markers for tuberculosis, lupus vulgaris—phlycten, scrofuloderma, BCG scar, tuberculids
   - Sacral dimple—spina bifida
   - Salmon pink maculopapular rash (collagen vascular disease)
   - Multiple burns (syringomyelia)
   - Vasomotor changes—coldness/oedema on the affected part (autonomous disturbances)
   - Any obvious deformity—skeletal deformities and joint contractures in cerebral palsy

TABLE 11.5 Neurocutaneous Markers

Neurocutaneous Markers	Neurocutaneous Syndromes
Café au lait spots, axillary freckles	Neurofibromatosis
Telangiectasia	Ataxia telangiectasia
Adenoma sebaceum, shagreen patch, ash-leaf macules	Tuberous sclerosis
Haemangioma	Sturge–Weber syndrome
Tuft of hair	Spina bifida
Nevus	Linear nevus syndrome



FIGURE 11.1 Child with linear nevus syndrome. Note the nevus on forehead extending to nose in midline.



FIGURE 11.2 Café au lait spots in a child with neurofibromatosis.

7. Odour of the body—many metabolic disorders affecting the nervous system are associated with change in body odour (Table 11.6)



FIGURE 11.3 Haemangioma.

TABLE 11.6 Body Odour Associated with Neurological Disorders

Condition	Body Odour	Associated Neurological Disorders
Phenylketonuria	Musty odour	Progressive mental retardation
Maple syrup urine disease	Maple syrup	Seizures, mental subnormality, coma
Uraemia	Ammoniacal	Encephalopathy
Hepatic failure	Musty	Encephalopathy

CNS EXAMINATION

Any child in whom a neurological illness is suspected, a variety of tests are done depending on the age and maturity of the child. A systematic approach is needed as with any other examination, so that any part of the examination is not missed. Start with the cephalic end and proceed towards the caudal end. The functions of brain such as consciousness should be examined first, whereas caudal examination such as anal reflex should be examined in the last. A detailed CNS examination should be conducted including examination of the higher functions, all the cranial nerves, spinomotor and sensory system, cerebellum and the autonomic nervous system (ANS).

Higher Functions

Cognitive Functions

1. Level of consciousness (see Chapter 3, section *Consciousness*, page 20).
2. Orientation can be tested for time, place and person. Self-orientation is the ability of a person to estimate one's own position with regard to time, place and person. The child may be disoriented in CNS infections and organic psychosis.
   - Orientation in time—is the child able to tell the day, month, year without looking at a calendar? Is the child able to estimate the approximate time without looking at a watch?
   - Orientation in place—is the child aware of the surroundings he/she is presently in? Is the child aware of the place he/she comes from?
   - Orientation in person—can the child identify the persons around him/her?
   - Orientation to self—can the child tell his/her name and age?
3. Attention and concentration—attention is the cognitive process of selectively concentrating on one aspect of the environment while ignoring others. To test the attention, the child could be given a number and asked to do a sequential subtraction up to zero. Another way of testing attention is to say a five-letter word (for example 'water') and ask the child to spell it in a reverse manner.
4. Memory is the mental faculty that enables one to register, retain and recall previously experienced sensations, impressions, informations and ideas. The brain retains and uses the knowledge gained in the past. The various components of memory are given in Box 11.2. Different types of memory are as follows:
   (a) Immediate memory (working memory)—this consists of memory lasting for a minute or so. This can be tested by asking the child to reproduce a series of randomly selected numbers (numbers 1, 9, 7, 5, 2, 3 and 10) or names of three objects. Starting with series of three non-consecutive numbers,

BOX 11.2 Components of memory

- Registration—is recording the events or the names of objects. It is the ability to retain information. Say three names and then ask the child to repeat.
- Retention—ability to retain events in the mind so that it can be recalled when required.
- Recall—is to bring back the registered names or events. Ask the child to give the names of his school friends or relatives.

one number is increased each time until the child makes consistent errors in repeating. Most children are able to correctly repeat seven to eight numbers forwards and four to five numbers backwards. In organic dementia, immediate memory is impaired due to poor concentration and loss of ability to retain and recall. However, the distant memory is preserved.

(b) Recent or short-term memory—the child is asked to reproduce an event that happened few minutes back. For instance, the child can be asked to repeat a sentence told to him 5 minutes back; or he can be told names of three objects of different categories. After ensuring that the child has registered them, other tests should be performed. After approximately 5 minutes, the child should be asked to recall the names of those items. Normal child can do this correctly in three attempts or less based on his ability to retain and retrieve. A child with normal retention but impaired retrieval is able to pick the answers from a list but is not able to recall.

Korsakov's Psychosis—recent memory and orientation to time are disturbed. Confabulation is common wherein the patient tries to fill up the memory deficiency with other words. It is seen in children under 2 years of age, alcoholism and anterior hypothalamic lesions.

(c) Long-term memory or remote memory—this can be tested by asking the child to recall some events that happened long time back (many years). For instance, a child can be asked the place of residence 3 years back, or a college goer be asked the name of his first school.

5. Intelligence and judgement—intelligence is the capacity to understand and the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas and learn from experience. Judgement is the ability of a person to estimate a situation to arrive at some conclusion and accordingly decide the further course of action. This can be tested by asking the child how he would react in a given hypothetical situation.
6. Insight—lack of insight is associated with lack of contact with reality. It is seen in psychotic illness, hysterical disorders and anxiety states.
7. Rapport—is the child maintaining a normal relationship with others? This depends on the personality and mental attitude of the child.

Appearance and Behaviour

Appearance of the child gives clue about his neurological status. Note his dressing sense and personal hygiene. Self-neglect is seen in depression, dementia and other psychotic illnesses.

Behaviour is the way in which a person reacts to the internal and external stimulus. Note if it is normal or abnormal. This should be assessed in terms of attitude to self, relationship to others, level of independence, mood, fantasy life, religious beliefs, interests and hobbies.

Mood (Mental and Emotional State)

The child may be apathetic, irritable, anxious, excited, depressed, frightened, euphoric, alert, dull, not interested in surroundings, etc. The clinician should note if the emotions of the child are appropriate as per the circumstances or not. Some of the abnormalities of emotions are as follows:

- Anger—a strong feeling of displeasure or hostility
- Inappropriate laughing or crying—the child may cry after hearing a joke or may laugh after being punished. It may smile in severe depression
- Irritability
- Elation—the child may be happier than the circumstances would warrant

Speech and Language

Assessment of speech and language is very important in assessing the cognitive state of the child (Table 11.7). Speech is use of words. Various types of speech are given in Table 11.8. Language is communication of thoughts, feelings and instructions through a system of arbitrary signals such as words, gestures or written symbols. The language area is situated in cortical area in the left hemisphere in most people.

TABLE 11.7 Testing Various Components of Speech and Language

Components	Method of Testing
Fluency	Note the fluency with which the child talks. Ask the child to say words beginning with a particular letter in 60 seconds. If the number of words produced in 60 seconds is less than 12, the child should be considered as dysfluent.
Word output	Note whether the word output is affected or not.
Comprehension	See if the child obeys commands by understanding it. For instance, does he close the door when asked? • Whether able to comprehend written language? Impairment of comprehension of written language is called alexia. • Whether able to comprehend spoken language? Impairment of comprehension of spoken language is called word deafness. • Whether able to write? Impairment of writing is called agraphia.
Repetition	Whether able to repeat? Ask the parent/attendant to say a sentence and ask the child to repeat the same sentence.
Naming	Whether able to name? Ask the child to name an object such as a watch or pencil.
Reading	Whether able to read? Ask the child to read some text from a newspaper or a book. Write a command and ask the child to read it. Next observe if the child obeys the written command.
Writing	Whether able to write? Ask the child to write his/her name or ask the child to write a sentence. Dysgraphia—ability to write is lost Perseveration—repeated use of a particular word
Copying	Whether able to copy? Ask the child to copy a geometrical design. Is the child able to comprehend symbols?

TABLE 11.8 Types of Speech

Types of Speech	Clinical Examination/Description
Scanning	Separation of syllables of words (e.g., Hip po pota mus)
Slurred	Words not clear
Staccato	Scanning and explosion. No coordination of lip and tongue
Stuttering	The child faces difficulty in uttering the first phoneme or sound at the beginning of a conversation
Stammering	Repetition of phonemes at the beginning or during the course of speech that interferes with normal flow and rhythm
Nasal twang	Occurs in X cranial nerve palsy, cleft palate

Speech and language should be assessed under the following domains:

- Fluency—word outflow that is free from pauses or breaks
- Word output—in non-fluent aphasia, the word output is affected and the child struggles to talk. In receptive aphasia, the word output is unaffected
- Comprehension—ability of a child to ascribe appropriate and correct meaning to words and sentences
- Repetition—ability to repeat single word or list of words without errors. Ask the child to repeat the sentence told by the examiner
- Naming—is the child able to name objects correctly?
- Speaking—name an object such as 'watch' and 'pencil'
- Reading—ability to comprehend written language symbols
- Writing—ability to use written language
- Copying—ask the child to copy a geometrical design

Speech and Language Defects. They result in difficulty in communicating effectively with others. Various defects in process of speech are given in Table 11.9. The type of defect depends on the site of brain affected. Upper motor neuron lesions result in aphasia/dysphasia (partial lack of speech). Lower motor neuron lesions result in dysarthria.

TABLE 11.9 Various Defects in Process of Speech

Process Affected	Defects
Hearing	Deafness
Understanding/thought and word finding	Aphasia
Voice production	Dysphonia
Speech articulation	Dysarthria

- Aphasia—inability to use language in speaking, writing or comprehending. Complete or partial disturbance of language comprehension, formulation and expression results in lack of speech or inability to speak sensibly and fluently. There is disturbance in speaking, writing or comprehending. Partial lack of speech is known as dysphasia. Speech is affected when dominant hemisphere is affected. In infantile hemiplegia other hemisphere takes over, hence speech may not be affected. Types of aphasia are given in Table 11.10.
- Dysarthria—articulation defects that result in problems in pronunciation of words. The main types of dysarthria are given in Table 11.11. Different presentations of dysarthria are given in Table 11.12.
- Paraphasia—syllable or words are missing and replaced by substitutions. In literal paraphasia, letters are missing and replaced, for example, 'rer' for 'red'. In verbal paraphasia, words are missing and replaced. For example, 'idly' for 'dosa'.
- Neologism refers to use of nonsense words.
- Alexia—impairment of comprehension of written language.
- Word deafness—impairment of comprehension of spoken language.
- Agraphia—impairment of writing.

Abnormal Experiences, Beliefs and Perceptions

- Delusion—fixed false beliefs which are strongly held inspite of invalidating evidence. These beliefs continue despite the evidence to the contrary.
- Illusion—misinterpretation of stimuli. Illusion is an abnormal perception of real objects. The child may perceive a rope as a snake.
- Hallucination—recurrent and persistent thought which intrude the patient's mind despite the effort

TABLE 11.10 Types of Aphasia

Type	Features
Motor aphasia (Broca's aphasia or expressive)	The patient is able to comprehend the speech of others as well as of self. The patient is able to understand spoken words, able to obey commands, but not able to answer the questions. While speaking, the sentences are broken (*non-fluent aphasia*) but meaningful. For example, a child with Broca's aphasia may say 'cup white table' when he/she means, 'there is a white cup on the table'. When asked 'what is your name?' he is not able to answer but is able to write his name on request (*intact comprehension, impaired repetition*).
Sensory aphasia (Wernicke's)	The patient is not able to comprehend the spoken words in spite of the ability to hear normally. They cannot obey the verbal commands but are able to answer the written questions and reply to written words. It results in *fluent aphasia* with *impaired comprehension and repetition,* i.e., the child can talk fluently on its own but cannot repeat what is said to him.
Nominal	The child cannot name an object such as watch or pencil and is a component of many aphasias.
Conduction	The child is not able to repeat the words spoken to him/her. This is seen in arcuate fasciculus lesions. The patient will be able to hear, obey commands, write the dictated words, respond to written commands but they will not be able to repeat the spoken words (*fluent aphasia with impaired repetition but intact comprehension*), or not able to answer verbal questions.
Transcortical motor	There is *motor aphasia with intact repetition.* It results from infarction in the left frontal lobe where the language area is anomalously represented. There will be impaired auditory comprehension but repetition will be preserved. The speech will be fluent but semantically empty.
Crossed (transcortical sensory)	There is *sensory aphasia with intact repetition* due to infarction in the right frontal lobe where the language area is anomalously represented.
Global	Both Broca's area and Wernicke's area are affected. The patient neither comprehends nor answers questions. In this condition the patient neither understands verbal commands nor speak.
Anomic	It is seen in angular gyrus lesions. The child cannot name things. There is trouble in visual processing because visual impulses are not transmitted to Wernicke's region.

TABLE 11.11 Types of Dysarthria Based on the Site of Lesion

Dysarthria	Clinical Presentation
Cerebellar dysarthria	The child speaks slowly and deliberately.
Spastic dysarthria	Individual syllables are slurred. It is seen in children with cerebral palsy. This is associated with pseudobulbar palsy and brisk jaw jerk.
Bulbar dysarthria in bulbar palsy	There is non-specific slurring of speech. Pronunciation of consonants is difficult.
Cortical dysarthria	There is irregular hesitancy in word production. This is seen in lesions of left frontal and temporal lesions.
Pseudobulbar palsy	Speech is strangled and spastic. British constitution may be pronounced as 'Brizn conshishushion'

TABLE 11.12 Manifestations of Articulation Defects

Manifestations	Description
Substitution	Another sound is substituted for a sound ('tat' for 'rat')
Omission	Sound omitted ('ox' for 'box')
Insertion	An extra sound is added to the word ('too' for 'to')
Distortion	Sound is not correct and distinct

to get rid of it. It is an abnormal sensory perception of an object which does not exist. These are seen both in organic brain disorders and functional psychosis, and can be visual, tactile, olfactory, auditory, vestibular or related to taste.

- Déjà vu—seen in temporal lobe epilepsy. The patient feels that he is familiar with the environment although he is in a new environment.

Cranial Nerves

Examination of cranial nerves is important in localisation of brain stem lesions as all the cranial nerves, except olfactory and optic nerve, originate in brain stem. The different components of the cranial nerves, their examination and the findings in nerve lesions are summarised in Table 11.13.

First Cranial Nerve: Olfactory

The olfactory nerve carries smell sensation from the olfactory receptors in the nasal mucosa.

Testing the Nerve. This is a purely subjective test. Obstruction to the nostrils due to common cold or any other cause should be ruled out prior to testing. The child's ability to appreciate smell is tested in each nostril separately with the other nostril compressed and occluded, and the eyes kept closed. Keep the substances near the nostril to be tested. Do not touch the nasal mucosa. Ask the child to identify the substance after two good sniffs. See if the smell perceived in both nostrils is same. Allow some time for the odour to disperse, and then repeat the test for at least two other odours. Use common substances such as almond, coffee, chocolate, oil of lemon, peppermint and asafetida which are familiar and can be easily appreciated. Do not use irritants or substances with pungent smell, as it may stimulate the trigeminal nerve and give a false impression of a normal test even if the olfactory nerve is affected.

Newborn. The baby turns the face towards the smell of breast milk. It is uncomfortable if an offending smell is present.

Lesions. Defects of olfaction are as follows:

- Anosmia—absence of smell. It occurs in head injury involving cribriform plate, tumours (pituitary tumour, frontal lobe glioma, olfactory groove meningioma), frontal lobe abscess and raised intracranial tension (ICT).
- Parosmia—altered smell with illusions and hallucinations of smell, smell is distorted and unpleasant. It can occur due to local causes in nose or head injury.

Second Cranial Nerve: Optic

Anatomy. The optic nerve is formed by the axons of the cells of the ganglionic layer of retina. It leaves the orbital cavity through optic foramen and unites with the optic nerve of opposite side to form the optic chiasma. In the chiasma, the fibres from the medial side of retina cross to opposite side, while the fibres from the lateral side continue on the same side and form the optic tract. Most of the fibres of optic tract reach the lateral geniculate body. Few fibres that are concerned with light reflex leave the optic tract and pass to the oculomotor nuclei on both sides via the pretectal nucleus and superior colliculus. From the lateral geniculate body, the fibres pass as optic radiation and terminate in the visual cortex.

TABLE 11.13 Clinical Examination of Cranial Nerves

Cranial Nerves	Components	Examination	Clinical Findings in Nerve Lesions
I—Olfactory	Sensory	Test the ability to appreciate smell in each nostril separately with closed eyes	Anosmia—loss of smell Parosmia—perversion of smell, distorted and unpleasant
II—Optic	Sensory	Gross vision • Test if the child recognises parents/objects/strangers • Test whether child smiles at mother or not	Not smiling at the mother, blank staring, unresponsive to facial expressions/visual threats, not following objects or a light
		Visual acuity • Snellen chart, tumbling E chart or Cardiff cards for distant vision • N chart, Jaeger's chart, Cardiff near cards for near vision	Not able to see distant things clearly in short-sightedness and near things in long-sightedness
		Visual field—test by confrontation method and perimetry	Visual field defects
		Colour vision—test by Ishihara chart and Precision vision 16 (PV 16) test	Inability to recognise different colours
		Examination of fundus by ophthalmoscope or slit lamp	Evidence for papilloedema, chorioretinitis
	Reflexes	Pupillary reflex—reaction to light	Pupillary constriction to direct light reflex is absent but responds to consensual light reflex from the normal eye
		Menace reflex—the fingers are taken towards the eyes. There is blinking or withdrawal of the head away from the stimulus	Absent
III—Oculomotor	Motor	Observe the eye at rest in primary position of gaze	Drooping of eyelids (ptosis) Dilated pupil Divergent squint
		Ask the child to follow objects. Observe the movements of eye in all directions	Decreased movements of eye ball (except abduction of eye caused by lateral rectus and downward movement of adducted eye by superior oblique)
		Doll's eye movement—turn the head to one side. When the brain stem is intact, the eye balls will move in the direction opposite to that of head movement	Presence of Doll's eye movements indicates supranuclear lesions or an intact brain stem
	Reflexes	Direct light reflex—seen in the eye in which the bright light is shined	Constriction of pupil of the same eye is absent
		Consensual light reflex—seen in the opposite eye in which the bright light is shined	Constriction of pupil of the opposite eye is absent
		Accommodation reflex—ask the child to look at a distance. Now ask him to look quickly at a near point	On convergence of eye balls, constriction of pupil is absent
IV—Trochlear	Motor	Ask the patient to look at the nose (downwards movement of the adducted eye)	The child is not able to see downwards with adducted eye

(Table continued)

TABLE 11.13 *(Continued)*

Cranial Nerves	Components	Examination	Clinical Findings in Nerve Lesions
V—Trigeminal	Sensory	Check the sensations over the face (except for a small area over the angle of jaw)	Absent sensations
	Motor	Ask the child to chew something to check the muscles of mastication	Deviation of jaw on chewing, difficulty in chewing
	Reflexes	Corneal reflex—touch the cornea with a cotton	Blinking of eyes is absent
		Conjunctival reflex—touch the bulbar conjunctive with a cotton.	Blinking of eyes is absent
		Jaw jerk—place the thumb over the lower jaw and tap over it with the jaw partially open	Jaw jerk is absent in LMN lesions It is exaggerated in UMN lesions
VI—Abducent	Motor	Ask the patient to look laterally	Not able to see laterally Convergent squint
VII—Facial	Motor	Inspection of the face	Obliteration of nasolabial furrow Deviation of angle of mouth to the opposite side Drooling of saliva on the same side
		Ask the patient to close the eyes tightly (orbicularis oculi)	Inability to close the eye tightly
		Ask the patient to wrinkle the forehead	Absence of wrinkles on the forehead on the affected side
		Ask the patient to blow (buccinator)	Inability to blow air
		Ask the patient to whistle (orbicularis oris and buccinators)	Inability to whistle
		Ask the child to show his teeth	Deviation of angle of mouth to the opposite side
		Eversion of lower lip (platysma)	Eversion of lower lip weak or absent
	Sensory	Check the taste sensations in anterior two-thirds of the tongue	Absent
	Reflex	Facial reflexes—sucking, corneal, conjunctival reflexes	Absent
VIII—Vestibulo cochlear	Cochlear (sensory)	Watch test for hearing—place a watch	Not able to hear ticking of watch or crumpling of paper near the ear
		Rinne's test—normally, it should be positive, i.e., air conduction > bone conduction	Negative (bone conduction > air conduction)
		Weber's test—place the vibrating tuning fork over the glabella. The sound will be perceived equally on both sides in normal children	Central (when both ears are affected) Lateralised to the affected side (when one ear is affected)
	Vestibular (sensory)	Calorie test—cold water and warm water are irrigated into the external auditory meatus Normal—positive Cold water—nystagmus to opposite side Warm water—nystagmus to same side (*Remember COWS: cold—opposite side, warm—same side*)	Negative in vestibular nerve lesions Cold water—nystagmus to same side Warm water—nystagmus to opposite side
		Unterberger's test—ask the patient to hold the hand forward and do walking movements	The patient sways towards the side of labyrinthine lesion
		Tandem walking—ask the patient to walk in a straight line with arms held forwards and eyes closed	The patient sways towards the affected side

(Table continued)

TABLE 11.13 *(Continued)*

Cranial Nerves	Components	Examination	Clinical Findings in Nerve Lesions
IX—Glossopharyngeal	Sensory	Taste—check for taste sensation in posterior one-third of tongue	Absent (ageusia)
	Motor	Muscle—stylopharyngeus	Paralysis of stylopharyngeus—not seen clinically
	Reflex	Palatal reflex—ask the child to say 'Ah'	Pharyngeal/gag reflex—palate is immobile
X—Vagus	Sensory	Palatal and pharyngeal sensation—test by touching the palate and pharynx with a swab	Absent sensations
	Motor	Inspection—position of uvula at rest	Uvula in the midline
		Ask the child to say 'Ah' and note the palatal movements.	Palate remains flat or immobile on the affected side
		Ask the child to speak	Nasal twang in voice
	Reflex	Gag reflex—touch the posterior pharynx with a cotton	Absent contraction
		Pharyngeal reflex—touch the posterior pharynx, base of the tongue and tonsillar fossa with a cotton swab. Normally there is retraction of tongue, elevation and contraction of pharynx and elevation of the palate.	Absent reflex
		Palatal reflex—palatal elevation as a response to stimulation of soft palate with a swab	Reflex contraction of palate
XI—Spinal accessory	Motor	Inspect neck muscles	Wasting Shoulder drooping
		Trapezius—ask the child to shrug the shoulders	The child is not able to shrug the affected shoulder
		Sternocleidomastoid—ask the child to turn the head to one side against resistance	The child is not able to turn the head to the opposite side of muscle paralysis
		Both sternocleidomastoids—ask the child to bow down the head (neck flexion)	The child is not able to flex the neck
XII—Hypoglossal	Motor	Inspection—observe the tongue at rest and during movement	Abnormal movements (fibrillations and fasciculations)
		Bulk of tongue	Wasting of tongue Atrophy
		Size of tongue	Small
		Palpation—palpate the tongue	Small contracted tongue in UMN and LMN palsy • Spastic (in UMN palsy) • Flaccid (in LMN palsy)
		Power—ask the child to protrude the tongue and look for any deviation of the tongue	The tongue deviates towards the side of lesion
		Power—ask the child to push the cheek with the tongue	The child is not able to push the cheek with the tongue

LMN—lower motor neuron; UMN—upper motor neuron.

Testing the Optic Nerve.

1. Gross vision—test the ability of the child to
   (a) recognise the parents (smile at parents),
   (b) recognise strangers (stranger anxiety),
   (c) recognise and reach out for familiar objects and
   (d) Follow objects.
2. Visual acuity—it is defined as the resolving power of the eye. Method of testing depends on the age of the child (Table 11.14).
   (a) Distant vision—the ability of the patient to see the objects at a distance is tested by using a Snellen chart. The chart contains letters of various sizes. The letters are large in the first row and progressively decrease in size in the lower rows. The largest letter subtends an angle of 5 min at the nodal point if it is placed at a distance of 60 m from the eye. The letters in the consecutive row subtend 5 min at 36, 24, 18, 12, 9 and 6 m from the eye, respectively. The chart is placed at a distance of 6 m from the patient at the eye level. The patient is asked to read the letters in the chart from above downwards. Visual acuity is expressed as d/D, where d is the distance of the child being tested and D is the distance from which that letter should be read by a normal child. Each eye is tested separately, with the other eye closed. In severe visual impairment, visual acuity is assessed, as given in Table 11.15.
   (b) Near vision—it is tested by Times New Roman numeral tests, reduced Snellen chart (Snellen chart with reduced size of the letters) and Jaeger's chart. Young children who cannot read can be tested by picture or block matching.
      - Times New Roman numeral tests—the chart consists of different sizes of printing in Times Roman type with standard spacing as advised by Faculty of Ophthalmologists. The near vision is recorded as the smallest type which can be comfortably read with a note of the approximate distance at which the card is held.
      - Reduced Snellen chart—it is made by photographic reduction of standard Snellen chart types to approximately 1/17th of the normal size.
      - Jaeger's chart—it is placed at a distance of 30 cm from the patient. Graded size of letters of pleasing font type is used. The vision is recorded as the smallest font size that the child can read comfortably. If the visual acuity improves on pin-hole test, the impairment is not due to neurological causes but due to refractive errors.
3. Colour vision—the ability of the patient to identify the basic colours (red, blue and green) is tested. Significant defect in colour vision is seen in diffuse optic nerve involvement as occurs in compressive or demyelinating lesions. Perception of red colour is affected first. Colour vision is tested by one of the following methods:
   (a) Isochromic charts (Ishihara charts)—these consist of dots in primary colours on similar backgrounds to make numbers or recognisable patterns, which can be identified by normal children. In children with colour blindness, these numbers or patterns cannot be identified.

TABLE 11.14 Visual Acuity

Age	Test
<4 years	Ability to follow objects
>4 years	E chart, picture or block-matching
Older children	Snellen chart—for distant vision Jaeger's chart—for near vision

TABLE 11.15 Assessment of Visual Acuity in Severe Visual Impairment

Finding	Assessment
Able to count fingers (CF) shown before him but not able to read any of the letters from the Snellen chart	CF+
Not able to count the fingers but able to appreciate the hand movements (HM) before him (no CF)	HM+
Not able to appreciate the hand movements but able to appreciate light (no HM)	PL+
Not able to appreciate the light, no perception of light (PL)	No PL

(b) Holmgren's wools—the child is asked to match a series of colours from coloured wools.

4. Visual field—it is defined as that portion of the space within which objects are simultaneously perceived while the eye is steadily fixed. The periphery of the normal visual field varies in radius with the direction (Table 11.16). The visual field is limited by the margins of the orbit, nose and cheek. Method of testing varies with the age of the child (Table 11.17) and is as follows:

   (a) Confrontation method—in this method, the visual field of the child is compared with that of the examiner. The patient and the examiner sit face to face at a distance of 1 m from each other with their eyes at the same level. The examiner closes his right eye and asks the patient to close the left eye. The patient is asked to fix gaze at the examiner's eye. The examiner brings his fingers with darting movements (or a red-coloured object of 3 mm size) from the periphery to the centre (Fig. 11.4). This is because moving objects are better appreciated than the static objects in the peripheral field. The fingers should also lie midway between the examiner and child.

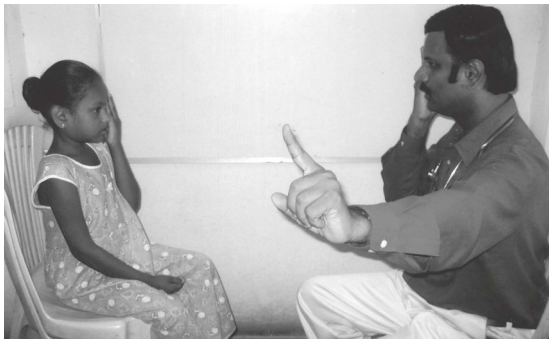


FIGURE 11.4 Confrontation method for visual field testing.

The point at which the patient is able to appreciate the moving finger is noted. This is compared with the point at which the examiner is able to note the finger. The difference in the examiner's ability to appreciate the movement compared with that of the patient gives the approximate abnormality of the field of vision.

(b) Perimetry—it is the quantitative analysis of the visual field and is used for diagnosis of visual defects (Table 11.18).

- Humphrey's automated perimetry is used in patients of glaucoma and certain neurological conditions affecting the optic nerve. In this method, repeated light stimuli of different intensities are given in different parts of visual field and are charted on the basis of patient's perception.
- Goldmann perimeter is used to evaluate both central and peripheral fields.
- Bjerrum tangent screen is used for evaluation of central visual field only.

TABLE 11.16 Normal Visual Field Radii in Different Directions

Periphery of Visual Field	Visual Field Radius
Superiorly	60°
Nasally	62°–65°
Inferiorly	75°
Temporally	105°–109°

Note that the visual field increases in radius clockwise—superiorly, nasally, inferiorly and temporally.

TABLE 11.17 Visual Field Testing at Different Ages

Age	Test
<3 years	Cannot be tested
>3 years	Confrontation test
>7 years	Perimetry

TABLE 11.18 Visual Field Defects

Type of Field Defect	Area of Decreased Visual Sensitivity
Central scotoma	Point of fixation
Paracentral scotoma	Adjacent to and not including the point of fixation
Caecocentral scotoma	Point of fixation and blind spot (optic disc area)
Altitudinal field defect	Upper or lower half of the field

5. Reflexes
   (a) Pupillary light reflex—a normal pupillary light reflex consists of contraction of pupils to light and depends on the integrity of afferent (optic nerve), centre (pretectal region in the brain stem) and efferent (oculomotor nerve) components. It is best tested in a dark room with the patient looking at a distance to avoid pupillary constriction due to accommodation reflex. Each eye is examined separately. Pupillary reflex is of two types:
      - Direct reflex—bright light is shone in one eye and pupillary constriction is seen in the same eye.
      - Consensual reflex (indirect pupillary reflex)—bright light is shone in one eye and pupillary constriction is seen in the opposite eye. The opposite eye should be shielded from light to avoid direct reflex. The constriction of the pupils of the opposite eye occurs because of the bilateral innervation of the Edinger–Westphal nucleus of the third nerve. (Fig. 11.5).

   (b) Menace reflex—it is used to test vision in children who are very small, uncooperative (e.g., aphasic patients) or totally bedridden. The finger of the examiner is suddenly brought towards the patient's eye. It is ensured that there is no air current created as a result of this movement. An air current causing closure of the eyes may give false-positive results. If the patient's vision is normal, moving a finger close to the eye will result in blinking of the eye. Hence, presence of menace reflex denotes normal vision grossly. Any condition with loss of vision will lead to absence of this reflex. Absence of menace reflex in the presence of normal pupillary reflex implies a lesion in the visual pathway after the pupillary reflex fibres cross the superior colliculus.
   (c) Accommodation reflex—it refers to contraction of pupils and convergence of eyeballs that occurs when a person suddenly focuses on a nearby object after having focused on a distant object. This is mediated from the retina via the accommodation reflex pathway (Fig. 11.6). Accommodation reflex may be present in the absence of light reflex due to lesion in the tectal region. This is called *Argyll Roberson pupil.*

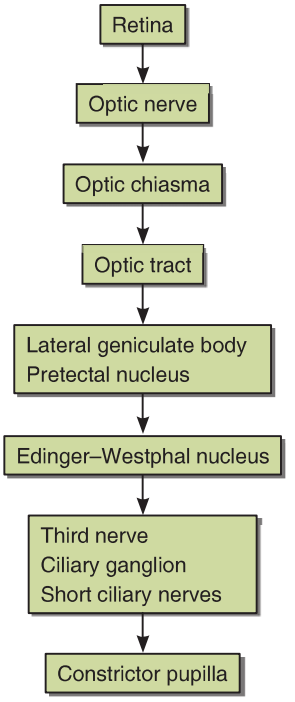


FIGURE 11.5 Light reflex pathway.

6. Fundus—this is examined by an ophthalmoscope in a dimly illuminated room with the pupils dilated and eyes fixed at a distance. Use the right eye for examining the right eye and the left eye for examining the left eye. The clinician should look for optic disc (shape, colour, edges, size and optic cup), vessels, retina and macula. In papilloedema, the disc is abnormally red and margins are blurred especially at the upper and lower margins. Physiological cup is obliterated and retinal veins are distended. It occurs due to raised ICT. In pseudo-papilloedema, disc appears swollen but the vessels are not engorged and the child is asymptomatic. Optic atrophy may be due to primary or secondary causes and should not be missed.

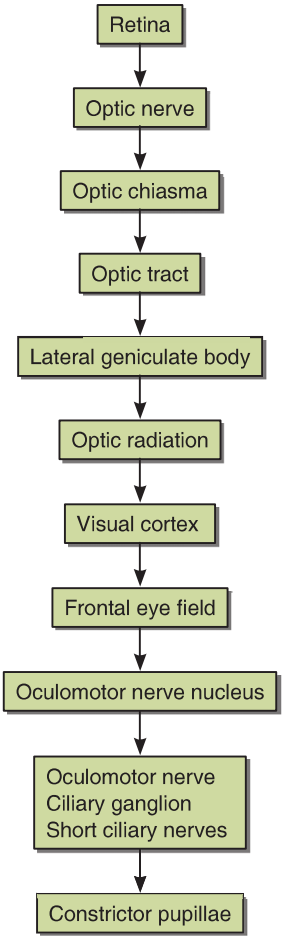


FIGURE 11.6 Accommodation reflex pathway.

Third Cranial Nerve: Oculomotor

The third, fourth and sixth cranial nerves are usually tested together. Any abnormal findings such as ptosis, squint and nystagmus should be noted in the primary position of gaze. The following features should also be checked:

1. Eye movements—these are controlled by the extraocular muscles. All of these are supplied by the third cranial nerve except the lateral rectus and superior oblique (Table 11.19). To test the eye movements, the patient is asked to look in all the directions without moving the head. In comatose patients, eye movements can be tested by *Doll's eye* manoeuvre. Eyeballs move in a direction opposite to the direction of passive movements of head. Some types of eye movements are as follows:
   - Nystagmus—rhythmic involuntary movements of the eye defined by the direction of fast movements.
   - Pursuit movements—slow movement of the eyes which depend on the fovea and the occipital cortex.
   - Saccadic movements—fast movements of the eye that depend on frontal lobes and pontine gaze centres. These can be elicited by holding two objects at about 30° apart and asking the child to look at each alternatively.
2. Eyelid movements—elevation of eyelids by levator palpebrae superioris which is supplied by oculomotor nerve. Lesion results in ptosis.
3. Pupils—look for size, shape, equality, regularity, reactions, position and symmetry. Pupil should be equal in size, round, regular, centred to the iris and should exhibit specific reflex responses (light and accommodation reflex).
   (a) Size—depends on the balance between the sympathetic and parasympathetic

TABLE 11.19 Nerve Supply and Action of Ocular Muscles

Muscle	Nerve supply	Actions
Superior rectus	III	Elevates abducted eye, adduction, intorsion
Inferior rectus	III	Depresses abducted eye, adduction, extorsion
Medial rectus	III	Adduction of the eye
Lateral rectus	VI	Abduction of the eye
Superior oblique	IV	Depresses adducted eye, abduction, intorsion
Inferior oblique	III	Elevates adducted eye, abduction, extorsion
Levator palpebrae superioris	III	Elevates upper eyelid
Constrictor pupillae and ciliary muscles	III	Constriction of pupils
Muller's muscle	Sympathetic	Elevates upper eyelid
Orbicularis oculi	VII	Closure of eyelid

Obliques act on the adducted eye, rectus acts on the abducted eyes.

innervations, levels of ambient illumination and the point at which the eyes are focused. The size can be measured using a pupillary gauge or a millimetre ruler. The size of normal pupils is 2–6 mm in diameter. In ambient light, it is 3–4 mm in diameter.

- Small pupils—pupils less than 2 mm diameter are considered as small. Pupils are small and poorly reactive at birth and in early infancy. They become normal by about the age of 7–8 years. Causes of small pupil are bright light, local causes (spastic or irritative miosis in corneal or intraocular foreign bodies, iridocyclitis, miotic drops, chronic anterior segment ischaemia, anterior or posterior synechia formation), Adie's pupil, paralytic miosis (oculosympathetic paralysis causing paralysis of pupillary dilator muscle), organophosphorus poisoning, pontine haemorrhage (pin point pupils) and Horner's syndrome.
- Dilated pupils (mydriasis)—pupils more than 6 mm are dilated. Dilated pupils can be unilateral or bilateral. Causes of bilateral dilated pupils are anxiety, fear, pain, myopia, drugs (anticholinergics, mydriatics), in children with light-coloured iris, midbrain lesions, comatose children, following cardiac arrest, cerebral anoxia, in terminal condition, dhatura poisoning. Causes of unilateral dilated pupils are third nerve palsy, Foster Kennedy syndrome (in frontal lobe tumours compressing one optic nerve, the pupils are dilated on the same side with papilloedema on the other side), upper brain stem lesion (fixed and dilated).

(b) Shape—normal shape is round with smooth, regular outline. The causes of abnormal shape are as follows:

- Congenital
- Trauma
- Iatrogenic/postsurgical
- Inflammatory
- Tumours
- Ectropion
- Ischaemia
- Idiopathic
- Horner's syndrome
- Argyll Roberson pupil—due to lesion in the pretectal region of mesencephalon. There is absent light reflex but accommodation reflex will be present
- Anterior or posterior synechia formation

(c) Equality of pupils—both the pupils should be equal in size. A difference of 0.25 mm is noticeable. Difference of ≥2 mm is significant. In anisocoria, pupils are unequal in size. This is more evident in bright light. It can be physiological or pathological. In physiological anisocoria, difference in size can be up to 1 mm. *Transient physiological anisocoria* may be due to Tournay pupillary phenomenon. In this phenomenon, when the child looks in extreme lateral gaze, the pupils of the adducting eye constrict whereas that of abducting eye dilate. The causes of *pathological anisocoria* are as follows:

- Idiopathic
- Third nerve palsy
- Adie's pupil
- Argyll Roberstson pupil
- Iritis
- Traumatic iridoplegia
- Pharmacological agents
- Iatrogenic causes

(d) Pupillary reactions

- Light reflex
- Accommodation reflex
- Ciliospinal reflex—it consists of dilatation of ipsilateral pupil in response to a painful stimulus (such as pinching the skin of neck or face). This is because cutaneous stimulation activates sympathetic fibres through connections with ciliospinal centre C8–T2. A normal response indicates the integrity of brain stem. It is absent in sympathetic lesions.

Light-near dissociation is seen in Argyll Robertson pupil and Adie's tonic pupil.

- *Argyll Robertson pupil:* It occurs due to lesion in pretectal area. The pupils do not respond to light but respond to accommodation.
- *Adie's pupil:* It is seen after damage to parasympathetic ciliary ganglion. It reacts poorly to light but better to accommodation. It is initially larger than the normal pupil, but becomes tonically constricted and redilates very slowly when exposed to dark.

Lesion of Third Nerve. The features that are seen in third cranial nerve palsy are due to involvement of levator palpebrae superioris (ptosis), extraocular muscles (diplopia, squint and defective movements) and constrictor pupillae and ciliary muscles. These are as follows:

- Absent light reflex—both direct and consensual light reflex are absent. The efferent fibres for the light reflex are supplied by the third cranial nerve. Hence, an intact oculomotor nerve is essential for a normal light reflex
- Accommodation reflex—absent
- Cannot follow objects
- Doll's eye movement—absent
- Drooping of the eyelids (ptosis)
- Diplopia
- Dilated pupil
- Divergent squint—due to unopposed lateral rectus muscle action (supplied by the abducent nerve)

Fourth Cranial Nerve: Trochlear

This nerve supplies the superior oblique muscle which is responsible for the downward movement of an adducted eye. The paralysis of this nerve leads to restriction of this movement so that the affected person has difficulty in reading books, looking at his/her own nose and climbing down stairs. It is usually tested together with III and VI nerves.

Fifth Cranial Nerve: Trigeminal

This nerve has both sensory and motor components. Sensory component carries pain, touch and temperature sensations over the face (except a small area over the angle of jaw). It has three divisions—ophthalmic (V1), maxillary (V2) and mandibular (V3).

The motor component supplies the muscles of mastication—masseter, temporalis and pterygoid.

Tests for Motor Functions.

1. Masseter muscle—the patient is asked to clench his teeth. The contracted muscle can be palpated over the angle of mandible. The contraction should be equal on both sides. Masseter is responsible for elevation of jaw.
2. Temporalis muscle—the suprazygomatic region is inspected for the muscle bulk of temporalis. The patient is then asked to clench the teeth. The contracted muscle can be palpated over the angle of mandible. The contraction should be equal on both sides. Temporalis is responsible for elevation of jaw.
3. Pterygoids muscle—in case of paralysis on one side, the jaw deviates to the same side. Lateral and medial pterygoids are tested by asking the patient to open the mouth against resistance. Lateral pterygoids are also tested by asking the patient to open the mouth and to move the lower jaw from side to side against examiner's resistance.

Tests for Sensory Functions

1. Ophthalmic division—touch, pain and temperature sensations should be tested over the following areas of face:
   - Both sides of root of the nose
   - Forehead and scalp up to the vertex
   - Cornea and conjunctiva (corneal reflex)
2. Maxillary division—touch, pain and temperature sensations should be tested over the following areas of face:
   - Cheek, upper lip and upper teeth
   - Front of the temple, side of the nose and mucous membrane of the nose
   - Skin and conjunctiva of the lower eyelid and the medial inferior quadrant of the cornea
   - The upper part of the pharynx, the roof of the mouth, part of the soft palate, the tonsils
3. Mandibular division—touch, pain and temperature sensations should be tested over the following areas of face:

- Lower part of the face, the lower lip, the ear, the tongue and the lower teeth
- Both sides of chin (except the angle of mandible which is supplied by C_2 segment of the spinal cord)

Reflexes

1. Corneal reflex—the afferent pathway of the reflex is by the trigeminal nerve and the efferent pathway is by the facial nerve. The reflex centre lies in pons. The child is asked to look upwards. The test is done by touching the lateral margin of the cornea with a wisp of cotton just lateral to the pupil on either side. The patient blinks on both sides irrespective of which side is touched. The procedure should be explained to the child beforehand or else the child may be scared. Care should be taken not to touch the central part of the cornea or rub/wipe it harshly as this may cause ulceration (especially if corneal sensations are not normal).
2. Jaw jerk—both the afferent and efferent pathways of the reflex are by the trigeminal nerve and the reflex centre is in pons. The child is asked to open the mouth partially. The examiner places the left index finger below the lower lip in the midline. He then strikes that finger in a downward direction using a hammer (Fig. 11.7). The jaw jerk is seen as a minimal upward movement of the jaw. Often the jaw jerk may not be elicited even in normal children. In UMN lesions the jaw jerk is exaggerated.
3. Nasolacrimal reflex—the afferent limb of the reflex is via trigeminal nerve and the efferent limb is through the greater superficial petrosal nerve. The test is done by stimulating the nasal mucosa with a wisp of cotton. Stimulation of the nasal mucosa leads to reflex stimulation of tears, which is called the nasolacrimal reflex.



FIGURE 11.7 Jaw jerk.

Testing the Fifth Cranial Nerve in Newborn.

The fifth cranial reflex is tested in newborns by rooting reflex. When the cheek on one side is touched, the child turns towards that side.

Lesion of Fifth nerve

- Total loss of sensations over one side of face (except over angle of mandible which is supplied by C_2).
- Total loss of sensations over one or more main divisions of trigeminal nerve on one side of face.
- The salivary and lacrimal secretion may be diminished.
- Trophic ulcers in mouth, nose and cornea.
- Loss of corneal reflex.
- Weakness of muscles of mastication.
- Deviation of jaw to one side.
- Only touch sensation is lost in pontine lesions affecting the principal sensory nucleus. It is seen in pontine tumours.
- Loss of pain and temperature sensations with preservation of touch is called dissociative sensory loss. Lesion of descending root which descends into the spinal cord is seen in syringobulbia, tumours in the foramen magnum and bulbar vascular accidents.
- Thrombosis of posterior inferior cerebellar artery results in ipsilateral loss of pain and temperature over the face and contralateral loss over the body.
- Hyperaesthesia over all or part of the distribution of trigeminal nerve is seen in vascular lesions, herpes and rarely in syringomyelia.

Sixth Cranial Nerve: Abducent

This nerve supplies the lateral rectus muscle. Paralysis leads to loss of abduction of the affected eye. This leads to convergent squint due to the unopposed action of the medial rectus muscle which is supplied by the oculomotor nerve (Fig. 11.8).



FIGURE 11.8 Child with right VI and VII cranial palsy. Note the deviation of the right eye towards the medial side due to right lateral rectus palsy and unopposed action of right medial rectus. The child also has left-sided deviation of angle of mouth due to right facial nerve palsy.

Seventh Cranial Nerve: Facial Nerve

Peripheral Functions. These can be summarised as face, ear, taste and tear.

- Face—muscles of facial expression
- Ear—tensor tympani and stapedius
- Taste—taste sensation in the anterior two-thirds of tongue
- Tear—parasympathetic supply to lacrimal glands

Paralysis of the Facial Nerve. The nerve has a bilateral representation for the upper half of the face. The lower part of face is supplied by that part of motor nucleus which receives contralateral corticonuclear fibres. The paralysis can be due to a lesion at any level during the course of the facial nerve.

1. Supranuclear palsy (UMN lesion)—the lesion above the level of facial nerve nuclei causes a UMN or supranuclear palsy. It occurs due to involvement of pyramidal tract.
   - Only contralateral lower part of face is affected. The upper one-third of the face is spared because the neurons supplying it receive corticobulbar fibres from both cerebral cortices.
   - The UMN fibres from the lower part of precentral gyrus are concerned with voluntary movements (on command). Lesion of these fibres results in normal movements on smiling, talking, etc., but absence on command.
   - The UMN fibres originating in frontal lobe are concerned with emotional movements. Their lesion results in absence of movements on smiling, talking, etc. However, the child is able to retract the angle of mouth on command.
2. Infranuclear palsy (LMN lesion)—the paralysis due to any lesion at the level of facial nerve nuclei or below the level of these nuclei causes lower motor neuron or infranuclear paralysis.

Differences between supranuclear and infranuclear facial nerve palsy are given in Table 11.20.

Causes of Seventh Nerve Palsy. The most common cause of facial nerve palsy is Bell's palsy (idiopathic LMN palsy). Broadly, the causes are classified as follows:

1. LMN palsy
   (a) Unilateral LMN weakness
   - Bell's palsy (commonest cause)
   - Pontine vascular accidents
   - Lesions at the cerebellopontine angle
   - Herpetic lesions in its course through the temporal bone
   - Parotid tumours
   - Laceration of face

   (b) Bilateral LMN weakness
   - Sarcoidosis
   - Guillain–Barré syndrome
   - Myasthenia gravis
   - Myopathies
   - Dystrophia myotonica
   - Leprosy
   - Tuberculosis
   - Facioscapulohumeral muscular atrophy
   - Hypoxic ischaemic encephalopathy stage III
2. UMN palsy
   (a) Unilateral UMN
   - Cerebrovascular accidents
   - Demyelination

TABLE 11.20 Difference between Supranuclear and Infranuclear Facial Nerve Palsy

Features	Supranuclear Palsy (UMN Type)	Infranuclear Palsy (LMN Type)
Lesion	Above the facial nerve nucleus	At or below the level of nucleus up to the myoneural junction
Parts affected	Lower part of face. Upper face is spared due to bilateral representation	One half of the face is involved (lower and upper)
Movements affected	Voluntary movement Emotional movements	All movements on the affected side will be lost
Bell's phenomenon	Never occurs	Bell's phenomenon—present
Facial muscles	Not atrophied	There may be fasciculation or muscle atrophy on the affected side
Taste sensation	Taste sensation is preserved	Taste sensation may be lost
Corneal reflex	Preserved	Lost
Associated features	Always associated with same-sided hemiplegia	May be an isolated phenomenon (Bell's palsy) and if associated with hemiplegia; it is always crossed
Hyperacusis	Not present	Present if the nerve to stapedius is affected
Plantar response on the paralysed side of face	Extensor	Flexor (may be extensor on the opposite side)

LMN—lower motor neuron; UMN—upper motor neuron.

- Tumours (supratentorial lesions)

(b) Bilateral UMN

- Pseudobulbar palsy
- Emotional paralysis

Clinical Evaluation. Facial nerve is tested by asking the patient to do various manoeuvres as given in Table 11.21. The child should be assessed for following features:

- Is there a general medical syndrome (e.g., hyper/hypothyroidism, Cushingoid syndrome)?

TABLE 11.21 Testing the Facial Nerve

Test	Observation in Normal Cases	Muscle Involved
Ask the child to look above	Wrinkling of forehead	Frontal belly of Occipitofrontalis
Close the eyes	Tight closure, cannot be opened by using examiner's hands	Orbicularis oculi
Blow cheek	Full blown cheeks, air does not escape by pressing the full blown cheeks	Buccinator
Whistle	Good whistle sound	Orbicularis oris
Eversion of lower lip	Platysma becomes taut	Platysma

- Is the face expressionless or motionless?
- Are there abnormal movements of the face?
- Look at the symmetry of the face—note nasolabial folds and wrinkles on forehead (Figs. 11.8 and 11.9).
- Watch spontaneous movements—smiling and blinking.

Voluntary and emotional movements

1. Symmetry of face should be checked while the patient looks up at the ceiling by raising the eyebrows with the head kept straight. There is loss of frowning on the affected side in cases with LMN palsy.



FIGURE 11.9 Right-sided facial nerve palsy. Note the inability to close the right eye, deviation of angle of mouth to left side and right-sided loss of nasolabial furrow.

2. The patient is asked to close his eyes tightly.
   - The eyes are partially open on the side of the nerve palsy.
   - Try to open the eyes with the patient attempting to close. It is normally difficult to open the eyes but can be easily opened in patients with facial nerve palsy.
   - Bell's phenomenon—the eyes roll upwards when the patient attempts to close the eyes (Fig. 11.10).
3. The patient is asked to inflate the cheeks with air against a closed mouth. The patient is unable to do so, or the air can be made to escape easily from the side of weakness or paralysis by tapping the affected side.
4. The patient is asked to whistle. He is unable to do so.
5. The patient is asked to show teeth.
   - The angle of mouth deviates towards the normal side.
   - There is obliteration of nasolabial fold on the affected side.
6. Spontaneous facial movements should be checked during smiling, talking, crying, etc.

Testing the sensory functions

The taste sensation in the anterior two-thirds of the tongue is tested in each half separately. The child is asked to protrude his tongue and tested for sweet, salt, sour and bitter tastes separately after rinsing. The taste sensation is impaired in facial nerve palsy.



FIGURE 11.10 Bell's phenomenon in a child with right facial nerve palsy.

Lacrimation

Schirmer's test—it can be used to measure the production of tears in lesions of facial nerve at or above the level of geniculate ganglion. There is loss of lacrimation on the affected side. Blotting paper is kept underneath the lower eyelid and the amount of moisture is measured.

Reflexes

- Corneal reflex (afferent—trigeminal nerve, efferent—facial nerve)
- Conjunctival reflex (afferent—trigeminal nerve, efferent—facial nerve)
- Stapedial reflex—a loud noise causes contraction of the stapedius muscle and thereby reduction in the sound transmission. In cases with stapedial palsy, this protection is absent and there is hyperacusis (hypersensitivity to noise), especially for low tones (afferent pathway—vestibulocochlear nerve, efferent pathway—facial nerve)

Bell's Palsy. It is named after Sir Charles Bell and is also known as Antoni's palsy. It is an idiopathic unilateral LMN type of facial nerve palsy, not associated with other cranial neuropathies or brain stem dysfunction. Incidence is 15–40/10,000. There is no sex predilection and it affects all ages. Aetiology is not known. It develops abruptly in about 2 weeks after a systemic viral infection (Epstein–Barr [EB] virus in 20%). It is also associated with Lyme disease, herpes, mumps, etc.

Pathophysiology:

- Postinfectious allergic or immune demyelinating facial neuritis and not due to active viral invasion
- Oedema occurs in facial nerve in the narrowest part of the facial canal
- Ischaemia due to compression of the facial nerve by oedema
- Site of the lesion—at the meatal origin of the fallopian canal (Fisch's physiologic bottleneck)

Investigations:

1. Magnetic stimulation of the nerve
2. Evoked electromyography
3. Neuroimaging studies—CT scan to rule out other causes such as tumours
4. Facial nerve biopsy

- Lymphocytic infiltration
- Fragmentation of myelin
- Demyelination and chromatolysis of facial nuclear cells
- Oedema of the facial nerve

Treatment:

- Supportive—eye care
- Steroids—prednisolone in a dose of 1 mg/kg/day for 5 days tapered over next 15 days
- Antivirals—acyclovir and famcyclovir (limited benefits)
- Stimulation—nerve stimulation
- Self-training
- Surgical—surgery to decompress the facial nerve is recommended occasionally for patients with poor prognosis (persistent paralysis). If indicated, the surgery should be done within 14 days from the onset of symptoms

Prognosis:

- More than 80% patients recover spontaneously in 2–12 weeks
- The recovery is poor if there is reduction in action potential of the facial muscle after the first week
- Aberrant innervation may develop during recovery. The eyes may close when the mouth is shut. Tearing of the eyes during salivation (crocodile tears) may also be seen

Eighth Cranial Nerve: Vestibulocochlear

It has two divisions—cochlear and vestibular.

1. Cochlear division—it is concerned with hearing and is examined by the following tests:
   (a) Rinne's test—this test is done with a tuning fork of 512 Hz. The examiner strikes the tuning fork on a rubber pad and holds it to the ear till the patient ceases to hear the vibrations. This gives the air conduction threshold. Immediately after the patient says he/she cannot hear the sound the examiner should place the base of the vibrating tuning fork on the mastoid area and see if the patient can appreciate the vibrations (Table 11.22).
   (b) Weber test—the tuning fork is placed in the midline. The examiner strikes the fork on a rubber pad and holds it against the forehead in the midline. Other sites where the tuning fork can be placed are mentum, upper incisors and nasion. The best response is seen when the fork is placed on the incisors, but for hygienic reasons it is usually not done. The child is asked to indicate whether the vibrations are heard equally in both ears or better in one ear. Lateralisation of the sound occurs towards the affected ear in conduction deafness and towards the normal side in patients with sensorineural deafness (Table 11.22).

TABLE 11.22 Tuning Fork Tests for Hearing

Condition	Rinne	Weber
Normal	AC better than BC	Vibrations heard similarly on both sides
Sensorineural deafness	Both AC and BC decreased	Vibration heard better on the normal side
Conduction deafness	BC is better than AC	Vibration heard better on the affected side

AC—air conduction; BC—bone conduction.

2. Vestibular division—it is concerned with sense of movement, position and balance. The tests for vestibular functions include:
   (a) Calorie test—with the patient in supine position, the head is raised and kept at 30° from the horizontal. The lateral semicircular canal is in vertical plane in this position. The child is asked to fix the eyes at a point. Water (at 30°C and 44°C) is irrigated into the external auditory meatus for a period of 40 seconds. There will be nystagmus in a child with normal labyrinth. Cold water results in nystagmus towards the opposite side, while warm water results in nystagmus towards the same side (Table 11.23). Abnormal response can be as follows:
      - No response—canal paresis
      - Directional preponderance—nystagmus is more in one direction. This occurs in brain stem lesions and posterior temporal lobe lesions
   (b) Romberg's test—the patient is asked to close the eyes with feet together in standing position. If the patient has vestibular nerve

TABLE 11.23 Calorie Test

Test	Normal Response
Cold water (one ear)	Nystagmus towards the opposite side
Warm water (one ear)	Nystagmus towards the same side
Warm water (both ears)	Tonic deviation upwards
Ice-cold water at 4°C (both ears)	Tonic deviation downwards

Remember COWS: cold—opposite; warm—same. Also, 'warm up' and 'cool down'.

dysfunction, he/she sways towards the side of lesion.

(c) Unterberger's test—the patient is asked to hold the hand forwards and do walking movements with the eyes closed. If the patient has vestibular nerve dysfunction, he/she sways towards the affected side.

(d) Tandem walking—the patient is asked to walk in a straight line with arms held forwards and eyes closed. The heel of one foot should touch the toes of the other foot in each step. In patients with vestibular lesions, the child tends to fall on the side of the lesion.

Testing in Newborn. Sudden loud noise elicits a startle response in the newborn. This is known as startle reflex.

Ninth Cranial Nerve: Glossopharyngeal

The examination of the glossopharyngeal nerve includes testing the motor, sensory and secretory functions of the nerve as well as the reflexes governed by it.

1. Motor—this nerve supplies the stylopharyngeous muscle, which together with pharyngopalatinus muscle (supplied by X cranial nerve) elevates the pharynx. Paralysis of stylopharyngeous alone is not evident clinically
2. Sensory—the taste sensation is tested over the posterior one-third of the tongue. The tongue is touched with anode which produces Galvanic current of 2–4 mA. There will be metallic taste. In lesions of the glossopharyngeal nerve, the sensations over the soft palate, posterior third of the tongue, tonsillar fossa and pharyngeal wall are absent
3. Reflexes
   (a) Palatal reflex
   - The afferent limb is glossopharyngeal nerve and efferent limb is vagus nerve
   - To test the reflex, the posterior part of the pharynx is touched with a cotton swab. This results in an elevation of the palate along with contraction of the ipsilateral soft palate and deviation of uvula
   - Position of uvula is central in bilateral lesions. There is deviation of uvula to the normal side

   (b) Pharyngeal reflex (gag reflex)
   - The afferent fibres for this reflex are carried by the glossopharyngeal nerve and the efferent limb is formed by the vagus
   - The reflex is tested by stimulation of posterior pharyngeal wall by a cotton swab
   - This results in elevation and constriction of pharynx

Testing in Newborn. The palatal movements are checked while the baby is crying. The IX nerve is usually tested together with the X cranial nerve.

Tenth Cranial Nerve: Vagus

It is a mixed nerve which receives sensory fibres from the viscera of thorax and abdomen and carries motor fibres to palate, pharynx and larynx.

Clinical Examination

1. Position of uvula—the patient is asked to say 'Ah' and the palate and uvula are checked. In normal nerve function, there is equal elevation of the palate on both sides with no deviation of the uvula. In patients with vagus nerve palsy, the uvula deviates to the opposite side due to pull by the muscle on the normal side.
2. Pharyngeal reflex (gag reflex)
   - The afferent fibres for this reflex are carried

by the glossopharyngeal nerve and the efferent limb is formed by the vagus.
- The reflex is tested by stimulation of posterior pharyngeal wall by a cotton swab.
- There will be elevation and contraction of pharynx.

3. Curtain sign—in unilateral paralysis, the posterior pharyngeal wall moves towards the normal side on phonation.

Lesion of Tenth Nerve

1. Vagus nerve palsy—the clinical features are as follows:
   (a) Nasal twang
   (b) Nasal regurgitation
   (c) Choking
   (d) Dysphagia
   (e) Hoarseness of voice due to vocal cord paralysis
2. Superior laryngeal nerve palsy—superior laryngeal nerve is a branch of vagus nerve which receives sensations from larynx above the vocal cords and carries motor fibres to cricothyroid muscle.
   (a) Unilateral paralysis does not cause any symptoms.
   (b) Bilateral paralysis results in relaxed vocal cords and hoarseness of voice.
3. Recurrent laryngeal nerve palsy—recurrent laryngeal nerve is a branch of vagus. In recurrent laryngeal nerve paralysis the following features are seen:
   (a) Sensory loss in the larynx below the vocal cords.
   (b) Motor—all the intrinsic muscles of larynx are affected except cricothyroid.
      - Unilateral recurrent laryngeal nerve paralysis—unilateral paralysis of abductor of vocal cord (crico-arytenoid posterior). The affected cord lies in midline.
      - Bilateral recurrent laryngeal nerve paralysis—vocal cord lies in the cadaveric position. Stridor or respiratory obstruction may be present.

Eleventh Cranial Nerve: Spinal Accessory

Spinal accessory nerve is a pure motor nerve. It has two components—cranial and spinal. Fibres of the cranial root supply the larynx and pharynx (along with vagus). Fibres of the spinal root supply sternocleidomastoid and trapezius muscle. Any lesion of this nerve leads to wasting of these muscles.

Sternocleidomastoid Muscle

- Function—this muscle is responsible for movement of the head towards the opposite side.
- Testing the muscle—turning the chin to one side against resistance tests the sternocleidomastoid muscle of the opposite side (Fig. 11.11).
- The action of the muscle is gauged by the prominence of the muscle.
- The muscles on both sides can be tested simultaneously by asking the patient to flex the head against resistance.

Trapezius Muscle

- Function—this muscle helps in shrugging the shoulders.
- Testing the muscle—the examiner stands behind the patient and keeps his hand on the patient's shoulder on the side to be tested. He then applies resistance over the shoulder and asks the patient to shrug the shoulder (Fig. 11.12). The muscle strength is compared to that on the opposite side and any weakness is noted.
- XI nerve palsy results in drooping of the shoulder on the side of the paralysis.



FIGURE 11.11 Testing the sternocleidomastoid muscle.



FIGURE 11.12 Testing the trapezius muscle.

Testing in Newborn. Traction response is absent when the child is pulled to sit.

Twelfth Cranial Nerve: Hypoglossal

The hypoglossal nerve is purely a motor nerve. It supplies the intrinsic and extrinsic muscles of tongue and the depressors of the hyoid bone. The extrinsic muscles of tongue include hyoglossus, styloglossus, genioglossus and geniohyoid. These muscles except genioglossus are represented bilaterally. In frontal lobe lesion only genioglossus muscle is affected.

Testing the Hypoglossal Nerve

- The patient is asked to put out the tongue and keep it out for some time. Any weakness or inability to protrude the tongue is noted.
- The examiner should also look for wasting, atrophy or deviation of the tongue to one side.
- The patient should be asked to keep the tongue inside the oral cavity in a relaxed state and any fasciculations or fibrillations should be noted. Fasciculations are caused by contraction of a group of muscle fibres, while fibrillations result from contractions of individual muscle fibres.
- The examiner should feel the muscle tone of the tongue and note whether it is normal, flaccid or spastic. The tone of the muscle is increased in pseudobulbar palsy (UMN palsy) and decreased in bulbar palsy (LMN palsy).
- The patient can also be asked to move the tongue sidewards on both sides or touch the inner side of cheeks on both sides with the tongue. Any weakness or inability to do it should be noted.

In patients with hypoglossal nerve lesion, the tongue deviates towards the side of the lesion. In facial nerve palsy there is apparent deviation of the tongue due to the deviation of the angle of the mouth. This should not be mistaken for hypoglossal nerve palsy. The patient may be asked to move the tongue from side to side or touch the cheek with the tongue on both sides. He would not be able to do so in hypoglossal nerve palsy.

Clinical features due to UMN and LMN lesions of hypoglossal nerve are given in Table 11.24.

Testing in Newborn. The examiner should look for shape, bulk of tongue and movements during sucking.

Motor System Examination

Bulk of Muscles

The muscles are assessed for size, shape and symmetry and compared on both sides.

Inspection

- Posture
- Wasting or atrophy—muscle is small, soft and flabby. The convexity of the muscle is lost. The bones and tendons become prominent
- Hypertrophy

Palpation. Wasted muscles are flabby.

Measurement. The circumference of the muscles should be measured and compared with the opposite side. Measurements should be done at identical points on both sides. The circumference of the

TABLE 11.24 Features of UMN and LMN Lesions of XII Nerve

UMN	LMN lesions
Small spastic tongue	Atrophy
Dysphasia	Fasciculations
Dysarthria	Mucous membrane intact, so folds are seen
Drooling	Tongue deviates to same side of lesion due to action of genioglossus of opposite side.

muscles are measured from sites equidistant from fixed bony prominences such as olecranon process in the elbow, acromion of the shoulder and tibial tuberosity for the lower limbs.

Tone of Muscle

The tone of a muscle is the state of continuous partial contraction even at rest. It may be normal, decreased (hypotonia) or increased (hypertonia) (Table 11.25).

Inspection

1. The muscle involved is lax and pendulous at rest in hypotonia. The hypertonic muscle appears more prominent with increased convexity when compared to its counterpart on the opposite side.
2. Posture—pithed frog posture in hypotonia. In hemiparesis, the affected lower limb is externally rotated. Hypertonia can present with decorticate, decerebrate or opisthotonic posture (Table 11.26). In children less than 2 years of age, the posturing is not a reliable finding as the brain is not fully developed.
   (a) Decorticate rigidity
   - Flexor posturing is seen in children with lesions above intercollicular level.
   - There is disinhibition of red nucleus. This results in facilitation of rubrospinal tract and disruption of lateral corticospinal tract.
   - Rubrospinal tract facilitates motor neurons in the cervical cord which supply the flexor muscles of the upper extremities.
   - Lateral corticospinal tract facilitates motor neurons in the lower spinal cord which supplies the flexor muscles of the lower limbs.
   - The effects of corticospinal and rubrospinal tract above the red nucleus result in characteristic flexion posturing of the upper extremities and extensor posturing of lower extremities.
   - Decorticate rigidity indicates damage to cerebral hemisphere, internal capsule, thalamus and midbrain.
   - The score in Glasgow Coma Scale is three.
   - Clinical examination shows arms flexed and bent inwards over the chest; elbows, wrists and fingers flexed; hands clenched into fists; legs extended and feet turned inwards.
   - Children with decorticate posturing may progress to decerebrate rigidity.

   (b) Decerebrate rigidity
   - Extensor posturing indicates brain stem damage below intercollicular level.
   - It is an indication of more severe damage as rubrospinal tract and red nucleus are also involved and the lesion is lower down in the brain stem.

TABLE 11.25 Assessment of Tone

Clinical Examination	Normal	Hypotonia	Hypertonia
Inspection—posture	Normal	Frog position	Stiffness
Palpation of muscles	Normal	Flabby	Rigid
Resistance to passive movements	Normal	Decreased	Increased
Range of passive movements	Normal	Increased	Decreased

TABLE 11.26 Assessment of Tone by Posture

Postures	Conditions
Pithed frog posture (floppy position, lies still)	Hypotonia
Decerebrate posture—stiff, extended extremities, trunk and head; elbow extended, wrist flexed and arms hyperpronated. It indicates that the pontine and vestibular nuclei are maintaining the posture.	Lesion at brain stem level (elimination of cerebral functions)
Decorticate posture—elbow flexed, wrist flexed, arms supinated and flexed, clenched fists, lower limbs rigid and extended. The body position is maintained by midbrain and red nucleus without inhibition by diencephalon, basal ganglia and cerebral cortex.	Lesion above midbrain
Bending of the body such as arc (opisthotonus) Pleurothotonus—lateral bending of the body Emprosthotonus—bending in a backwards direction	Tetanus, strychnine poisoning

- The damage is below the red nucleus, that is, midcollicular level.
- It is common in compression of midbrain and lesions in the cerebellum.
- Clinical examination shows arms extended by the sides, head arched back (Fig. 11.13).
- The score in Glasgow Coma Scale is two.

(c) Opisthotonus posturing—head and back are arched backwards.

Palpation. During palpation, the muscle should be felt between the forefinger and the thumb. Palpation findings in case of hypotonia include flabby and soft muscles, increased range of passive movements and decreased resistance to passive movements (e.g., flexion or extension of the elbow or knee or abduction of the hip without any voluntary resistance). In hypertonia, the muscles are firm on palpation and there is increased resistance for passive movements at the joints.

Shaking the Limbs. The assessment of tone by shaking the limbs is given in Table 11.27.



FIGURE 11.13 Decerebrate posture.

TABLE 11.27 Assessment of Tone by Shaking the Limbs

Limbs	Holding Limbs	Observation	Range of Movements
Upper limbs	Hold the arm below the elbow	Observe the degree of movement of wrist	Increased in hypotonia Decreased in hypertonia
Lower limbs	Hold the leg below the knee	Observe the degree of movement of ankle	Increased in hypotonia Decreased in hypertonia

Power

It is the force of contraction that can be generated by the contraction of each muscle. It denotes the strength of muscle.

Testing. To test power, the child should be observed while carrying normal activities such as walking, playing and dressing. Muscles of different parts can be tested as follows:

1. Upper limbs
   (a) Proximal—child should be asked to lift the arm above the head and comb the hair
   (b) Distal—these muscles are involved in fine motor activities such as writing, mixing of food, buttoning, dressing/undressing and eating
2. Lower limbs
   (a) Proximal—the child should be asked to get up from sitting position
   (b) Distal—these muscles are involved in walking with slippers held in the foot (holding the slippers while walking without slipping)
3. Neck—lifting the head
4. Trunk—getting up from supine position, turning in the bed

The child is asked to draw a circle above his reach; this will test all the four groups.

Grading of Muscle Weakness. Power should be graded according to the maximum power attained by contraction of the muscle, no matter how briefly this is maintained. Muscle power is graded conventionally according to the Medical Research Council (MRC) scale.

MRC grading of muscle weakness

Grade	Clinical examination
0	Complete paralysis total paralysis (no power)
1	Visible or palpable flicker or trace of contracture, not enough to move a joint
2	Able to move eliminating the gravity
3	Able to move against gravity but not against resistance
4	Able to move against partial resistance
5	Normal power

The MRC grading of power cannot be applied to the following muscles:

- Trunk muscles
- Muscle involved in hand grip
- Facial muscles
- Intrinsic muscles of limbs
- Muscle involved in finger grip
- Muscles of respiration
- Paraspinal muscles

Reflexes

Superficial Reflexes. These are muscle contractions that are evoked by cutaneous stimulation, that is, stroking the skin. These are summarised in Table 11.28 and include abdominal, corneal, conjunctival, cremasteric, plantar, scapular, anal and bulbocavernosus reflexes. Plantar reflex is discussed in detail as it can be elicited by several different methods. Superficial reflexes are absent in the following conditions:

- Lesion in the pyramidal tract
- Lesion above the level of reflex arc
- Lesion in the reflex arc

The causes of absent abdominal reflex are as follows:

- Obesity
- Lax abdominal wall
- Ascites
- Old age
- Laparotomy scar
- Pyramidal lesion
- Multiple sclerosis

Plantar reflex: The lateral border of the sole is stroked from the heel towards the ball of the great toe. Normal response is flexor. The following components are present:

- Contraction of tensor fascia lata
- Contraction of adductors of thigh and sartorius
- Adduction of four outer toes
- Plantar flexion of four outer toes
- Plantar flexion of big toe
- Dorsiflexion and inversion of ankle
- Withdrawal of the limb

The causes of absent plantar reflex are as follows:

- Pyramidal tract lesions
- S_1 lesion
- Paralysis of extensor hallucis

TABLE 11.28 Superficial Reflexes

Reflex	Method of Eliciting	Centre	Normal Response
Abdominal reflex	Stroke the skin over the abdomen from lateral to medial side	Spinal segments T_6–T_{12}	Muscles of abdomen contract
Cremasteric reflex	Stroke the upper and medial aspect of thigh	L_1, L_2	Testicle is pulled up due to contraction of cremasteric muscle
Plantar reflex	With the patient lying down, knee slightly flexed, thigh externally rotated, fix the ankle joint and stroke the lateral aspect of the sole	L_5, S_1	Flexion of great toe, flexion of other toes
Scapular reflex	Stroke the skin in the interscapular region	C_5–T_1	Contraction of the scapular muscle
Anal reflex	Scratch the perianal skin	S_3, S_4	Contraction of external anal sphincter
Bulbocavernous reflex	Pinch the dorsum of the penis	S_3, S_4	Contraction of bulbocavernous

- Spinal shock
- Thick sole

The causes of extensor plantar with flaccidity are as follows:

- Neuronal shock
- Coma
- Friedreich's ataxia
- Subacute combined degeneration of spinal cord
- Tabes dorsalis
- Transverse myelitis
- Conus medullaris lesions

Babinski's sign (upgoing plantar reflex): It can be elicited by stroking the lateral aspect of the foot. In positive Babinski's sign, there is contraction of tibialis anterior, hamstrings and tensor fascia lata. The components of Babinski's sign are as follows:

- Dorsiflexion of great toe
- Extension and fanning of other toes
- Dorsiflexion of ankle
- Flexion of knee
- Flexion of hip

In pyramidal tract lesions, there is an increase in the reflexogenic area. Hence, the reflex may be elicited even by stroking the skin high above in the leg. Other methods of eliciting plantar extensor reflex are as follows:

- *Oppenheim's sign* (shin-toe reflex)—heavy pressure is applied by knuckles or the thumb and index finger to the anteromedial surface of tibia from above downwards (from the infrapatellar region to the ankle on its medial side). The extensor response usually occurs towards the end of the stimulation.
- *Gordon's sign* (calf-toe sign)—squeezing, pinching or applying deep pressure to the calf muscles or tendo-achilles produces extensor plantar response.
- *Chaddock's sign*—extensor response is seen after striking the skin around lateral malleolus in a circular fashion.
- *Bing's sign* (pinprick-toe reflex)—pricking the dorsum of foot by a pin produces extensor response.
- *Moniz sign*—extensor response is seen after forceful passive plantar flexion of ankle.
- *Gonda sign* (Allen sign) (toe-pull reflex)—extensor response is elicited after forceful downward stretching or snapping of distal phalanx of either of the second or fourth toe.
- *Schaefer's sign* (Achilles-toe reflex)—deep pressure or squeezing over the tendo-achilles tendon produces extensor response.

Pseudo-Babinski's sign: The plantar response is extensor at birth. As the cortex develops, the pyramidal tract inhibits this extensor response, so the plantar response becomes flexor by 1 year of age. Any condition which inhibits the cortex or the pyramidal tract leads to a plantar extensor response. The plantar extensor response may be seen in the absence of pyramidal tract lesions in the following conditions:

- Voluntary withdrawal
- Plantar hyperaesthesia
- Strong or painful stimulus
- Extra pyramidal lesions
- Infants (age under 1 year)
- Deep sleep
- Post-ictal
- Sedative drugs
- Post-traumatic (e.g., in spinal shock)
- Following electroconvulsive therapy

Brissaud's reflex: Stroking of sole elicits contraction of tensor fascia lata which is a part of plantar extensor reflex. This is observed in patients with absent toe or amputated toe in whom the plantar extensor response cannot be seen by observing the great toe. In such cases, the examiner should look for the contraction of the tensor fascia lata.

Deep Tendon Reflexes. These reflexes are tested by striking a tendon which is partially stretched. To stretch the tendons, the part of the body where the reflex is to be elicited should be properly positioned. It is the tendon which should be stroked and not the muscle belly. Different deep tendon reflexes (DTRs) are summarised in Table 11.29 and include biceps reflex, supinator, triceps, knee jerk, ankle jerk and jaw jerk (Figs. 11.14 and 11.15).

TABLE 11.29 Deep Tendon Reflexes

Reflex	Spinal Segment	Elicitation	Response
Biceps reflex	C_5, C_6	Place the index finger of the left hand on the biceps tendon and gently strike over the finger with the knee hammer	Flexion at the elbow joint with visible contraction of the biceps muscle
Supinator reflex	C_5, C_6	Hold the arm midway between pronation and supination. Tap on the tendon of brachioradialis at the distal end of the radius	Contraction of brachioradialis with flexion of elbow. Slight flexion of fingers and contraction of biceps may also be present
Triceps reflex	C_6, C_7, C_8	Pull the arm across the chest by holding the hand with the elbow flexed to 90°. Tap on the triceps tendon	Extension of elbow with visible contraction of the triceps muscle
Knee jerk	L_2, L_3, L_4	In sitting position: with the legs hanging at 90° to the thigh, strike the quadriceps tendon with the knee hammer In supine position: place the left arm below the knee and strike the patellar tendon with a knee hammer	Extension of the knee due to contraction of quadriceps
Ankle jerk	S_1, S_2	a) Conventional method: with patient supine, place the lower limb in externally rotated position. With the knee and hip partially flexed and slight dorsiflexion at ankle, strike the Achilles tendon with the knee hammer b) Special method: patient takes knee-down position on a chair with both feet hanging out of the chair. A sharp tap is applied on tendo-Achilles calf muscles contract and plantar flexion of foot results	Planter flexion of the ankle with visible contraction of the calf muscle



FIGURE 11.14 Eliciting knee jerk.

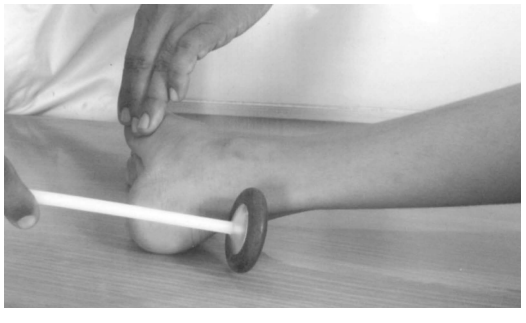


FIGURE 11.15 Eliciting ankle jerk.

The grading of DTRs is as follows:

Grades	Findings
0	Absent
1	Sluggish, obtainable with reinforcement
2	Readily elicitable, normal like normal ankle jerk
3	Brisk/increased like normal knee jerk
4	Clonus (sustained/ill-sustained)

Enhancement or reinforcement of DTRs: Reinforcement means making some strong voluntary muscular effort. This method is used to elicit DTRs when they cannot be elicited by routine manoeuvre. The purpose is to distract the child from voluntary suppressing the reflex. It is very important to remember that this phenomenon lasts for less than a second. So, the patient is asked to do the manoeuvre almost synchronously with the tapping of the tendon (the procedure must be demonstrated to the patient before tapping of the tendon). It should always be performed before declaring a tendon reflex as 'absent'. This can be done by

- clenching the teeth,
- making a tight fist of the hand other than the hand being tested and
- Jendrassik's manoeuvre—interlocking the fingers of both the hands and pulling them in opposite directions (Fig. 11.16).

Interpretation of DTRs: The DTRs may be normal, diminished or exaggerated (Table 11.30):

1. Diminished/absent reflexes—any lesion affecting the reflex arc leads to diminished or absent reflexes. Isolated loss of a reflex usually suggests radiculopathy. Symmetrical loss of reflex may be found in peripheral neuropathy. Reflexes may be absent if the patient is 'unable to relax' due to repeated stimuli.
2. Exaggerated DTRs—the reflexes are under an inhibitory control from the pyramidal tract. Any lesion to the pyramidal tract leads to the loss of this inhibition and exaggeration of the reflexes. Normally the control is complete by 1 year of age.
3. Clonus—stretching of the hypertonic muscles causes reflex contraction. If there are repeated contractions, it is called clonus. This occurs in pyramidal tract lesions. Clonus can be elicited at the patella and ankle.
   - Patellar clonus—with the child in supine position and leg extended, the patellar tendon is pushed down so that it is stretched (Fig. 11.17). Clonus can be elicited in pyramidal tract lesions. In normal newborn babies, the

TABLE 11.30 Significance of Abnormal Deep Tendon Reflexes

Reflexes	Conditions
Present	In health
Lost or diminished	LMN type of lesion—poliomyelitis, syringomyelia, peripheral neuropathy, tabes dorsalis UMN lesion—spinal cord lesion (stage of neuronal shock) Contracture of muscles and severe spasticity
Exaggerated	Pyramidal lesion, anxiety neurosis, nervousness, hysteria thyrotoxicosis, tetany, tetanus, multiple sclerosis, strychnine poisoning
Brisk	UMN lesions (pyramidal tract lesions) Infancy –cortical inhibition has not developed completely Hypoglycaemic coma (sometimes)
Pendular	Cerebellar lesion Chorea
Delayed relaxation (ankle jerk)	Myxoedema
Hung-up reflex (knee jerk)	Chorea Myxoedema
Inversion of supinator reflex—only finger flexion is present, all other components are absent	Lesion in C_5 segment



FIGURE 11.16 Jendrassik's manoeuvre.



FIGURE 11.17 Eliciting patellar clonus.

contractions may last longer giving a false impression of clonus.

- Ankle clonus—with the hip and knee flexed, the foot is dorsiflexed by applying pressure over the distal end near the toes and the stretch is maintained. In normal children, there will be few repeated plantar flexions, which will stop even when the stretch is maintained. In patients with pyramidal tract lesion, the plantar contraction will be repeated as long as the stretch is maintained.

Pathological Reflexes

- Babinski's sign (see section *Reflexes*, page 564).
- Hoffman reflex—hold the patient's relaxed hand with the wrist dorsiflexed and fingers partially flexed. The terminal phalanx of the middle finger is flicked downwards with the examiner's thumb by placing the finger on the volar aspect of the middle finger (Fig. 11.18). In cortical lesions, the tips of the other fingers flex and the thumb adducts.
- Wartenberg's sign (finger flexor reflex)—the fingers of the patient's hand to be examined should be flexed and interlocked to the examiner's flexed fingers. Pull in the opposite direction should be applied, so that the fingers are pulled against resistance (Fig. 11.19). Normally the thumb extends. In the presence of cortical lesions, the thumb adducts and flexes.
- Grasp reflex (forced groping reflex)—this is an extreme form of grasp reflex. An object is shown to the patient and then taken away. The patient with a contralateral frontal lobe lesion or diffuse bilateral disease involving both the hemispheres tries to grasp the object even in the absence of the object. This is not seen in normal children.
- Palmomental reflex—the skin is scratched along thenar or hypothenar eminence. This results in contraction of the ipsilateral mentalis muscle and uplifting of the leg. This is seen as puckering of the chin. Bilateral contraction can be seen in some normal children. Unilateral contraction is abnormal.
- Rossolimo's reflex—on tapping the pulp of the child's toes, there is flexion of the toes.
- Glabellar tap reflex—the afferent fibres are carried by the V nerve and efferent fibres are carried by the VII nerve. The hand is brought from behind and above the forehead and the glabella is tapped with the index finger (Fig. 11.20). Tapping the glabella from front is avoided as the fingers move towards the eye. It results in continuous blinking of the eye (menace reflex). Normally there are

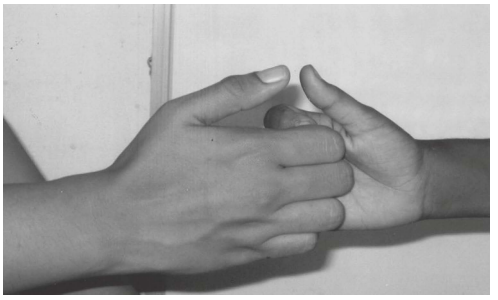


FIGURE 11.19 Method of eliciting Wartenberg's sign.



FIGURE 11.18 Hoffman's reflex.

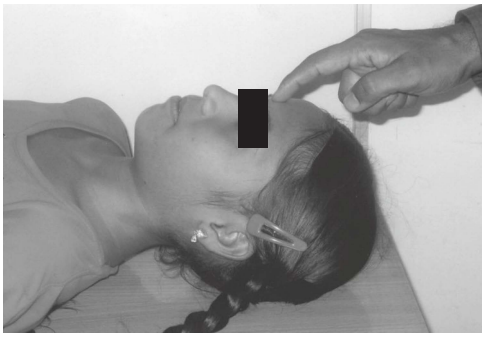


FIGURE 11.20 Glabellar tap reflex.

two to three blinks after which there are no blinks; more than that is considered abnormal. In children with diffuse degenerative lesions of the brain, the blinking persists for more than 4–5 times. Glabellar reflex is absent in the nerve lesions.

- Snout reflex—gentle pressure with the knuckles over the closed lip or between the upper lip and the nose causes puckering of the lip, primarily the lower lip, often with depression of lateral angles of mouth (contraction of orbicularis oris). This is seen in newborn babies and then disappears. In children with pyramidal tract lesions this is present. When exaggerated, the response is puckering with protrusion of the lips and sucking.
- Head retraction—a sharp tap just below the nose with the head bent slightly forward produces a quick involuntary backward jerk of the head. This is seen in bilateral corticospinal lesions and is absent in normal children.
- Rooting reflex—lips, mouth or head deviate towards the tactile stimuls.
- Mastication or wolfing reflex—an exaggerated response with automatic opening of mouth with smacking, chewing and swallowing of mouth when the object is brought near the mouth and does not touch the mouth.
- Chewing reflex—when tongue depressor is inserted into the mouth, there is clenching of the jaw which holds the tongue depressor.
- Finger flexion test ($C_{7, 8}$, T_1)—index and middle fingers of the examiner are kept over the proximal metaphalangeal joints and tapped. There will be flexion of fingers.

Coordination of Movements

Coordination can be tested in children above 6–7 years of age. This can be tested only when the power is more than grade IV. It depends on the integrity of the following components—cerebellum, extrapyramidal system and posterior column sensations (position sense). The tests for coordination should be done initially with the eyes open and then with the eyes closed. These should be performed on both sides and compared with each other.

1. Upper limbs—the tests to check coordination of movement in the upper limbs include the following:
   (a) Finger–nose test—the patient is asked to stretch the hand outside and touch the tip of the nose by the tip of the forefinger by bringing it towards the nose. Initially, this test is performed with open eyes and then with closed eyes. The test is also performed on the opposite side and the results of both the sides are compared. Any variation between both the sides should be noted. The variation is seen in children with unilateral cerebellar lesion or abnormal tone on one side. In posterior column lesions, this incoordination is exaggerated when the movement is done with the eyes closed.
   (b) Finger–finger–nose test—this test is performed in a similar way to finger–nose test. Here the patient is asked to touch the examiner's finger shown in front of him and then his nose. This should be done separately on both sides. This test is abnormal in cerebellar lesions.
   (c) Dysdiadochokinesis—it is defined as the inability of the patient to perform alternating movements. The patient is asked to do alternating movements such as clapping the hands with alternate pronation and supination. The examiner can also ask the patient to do alternate pronation and supination of the forearm flexed at the elbow. In children with cerebellar lesions, the child cannot perform these acts.
2. Lower limbs—the tests to check the coordination of movement in the lower limbs as follows:
   (a) Heel–knee test—the heel of one leg is placed on the opposite knee and is slided down the shin towards the ankle. This should be performed with eyes open. The examiner should look for any incoordination during this movement. The test should be repeated on the other side and the results should be compared. The child cannot perform this test on the side of affected cerebellum. The movements are irregular, with error in speed and direction resulting in side-to-side movements.

(b) The examiner may also instruct the patient to draw a circle in the air with his toe.
(c) Tandem walking (heel–toe walking)—the patient is asked to walk in a straight line with the heel of one foot placed near the tip of the toes of the other foot. This movement is abnormal in patients with cerebellar lesions and posterior column lesions.
(d) Romberg's test—the patient is asked to stand straight with both the feet kept close to each other. First the patient is asked to do this with the eyes open and then with the eyes closed. In cases with posterior column lesions, where the position sensation is lost, the patient falls on the side of the lesion when the eyes are closed. With the eyes open, the patient adapts to the loss of position sense by visual assessment of the position. When the eyes are closed or when the patient is in the dark, this adaptation is lost and the patient tends to fall down.

Stance and Gait

The posture is examined while the child is standing or walking and the associated movements of the arms are observed.

1. Stance—the child is asked to stand up straight with both feet close, first with eyes open and then with eyes closed. If balance deteriorates with eyes closed, it is a positive test and suggests lesion in proprioceptive pathway.
   (a) Thalamic astasia—in unilateral thalamic lesions, the child is not able to stand or sit which is out of proportion to the weakness or sensory loss.
   (b) Lurching on one side with eyes closed—cerebellar or sensory ataxia.
2. Gait—the child is asked to walk briskly for a distance of about 10 m, then turn to 180° and return back. The child is also asked to walk with heel to toe in a straight line. The length and width of steps is noted. Any abnormalities while the patient walks or turns around are observed. The gait varies with various lesions and gives a clue to the nature and type of the lesion. Types of abnormal gait are as follows:

(a) Spastic gait—slow, spastic, shuffling. In spastic gaits the child walks with a narrow base due to difficulty in bending the knees. The child walks by dragging his feet along the floor. This occurs in UMN lesions. The spastic gait can be hemiplegic or scissoring.
- Circumductory (hemiplegic) gait—this type of gait is seen in hemiplegia. As the patient is not able to use the affected lower limb, he leans to the opposite side and moves the lower limb at the hip joint in a circumductory manner. The affected upper limb is adducted at the shoulder and flexed at the elbow, wrist and fingers. There is abduction and internal rotation of the thigh, flexion of the hip and knee. The child walks on the toes with heel not touching the floor.
- Scissoring gait—this is seen in patients with infantile diplegia. There is scissoring (criss-crossing) of the lower limbs due to the adductor spasm.

(b) Equinus gait—is seen in any conditions associated with shortening of Achilles tendon. It is seen in spastic cerebral palsy and pseudomuscular dystrophy.
(c) Waddling gait—the affected child walks with a wide base and increased lumbar lordosis. The walk resembles that of a duck. The body sways from side to side with each step. The heels and toes are brought down simultaneously to the floor. This type of gait is seen in achondroplasia, bilateral coxa vara, bilateral slipped epiphysis and cerebellar disease.
(d) High stepping (slapping) gait—this occurs in cases with foot drop due to nerve lesions. The patient takes a high step in order to prevent the foot from dragging on the floor or tripping of the toes. Also when the foot comes down, the toes touch the ground first unlike the heel in normal persons. This type of gait is seen in tabes dorsalis, Friedreich's ataxia, subacute combined degeneration and syphilitic meningoencephalitis (rarely seen in adults).

(e) Stamping gait—in sensory lesions such as posterior column lesions, the patient cannot perceive the sensation of the floor while the foot is on the ground. The position sense is also lost and the patient does not know where the foot is. Hence, the patient raises the legs and places the foot forcibly on the floor as if he/she is stamping the floor. The intensity of stamping increases in the dark or when the eyes are closed because of the added absence of visual input.

(f) Cerebellar gait (staggering gait/ataxic gait)—the foot is raised high and lowered suddenly so that the whole sole strikes the ground. This gait is unsteady and the movements are not coordinated. The child also cannot walk on a straight line. It is seen in cerebellar lesions.

(g) *Marche à petit pas* (frontal gait)—this is short stepped, rapid tapping gait seen in bilateral diffuse cortical dysfunction. The gait resembles that seen in parkinsonism but lacks rigidity and bradykinesia. This is seen in normal pressure hydrocephalus and cerebral hemisphere dysfunction particularly involving frontal lobes.

(h) Apraxic gait—the integration of movements which is controlled by the frontal lobe is lost in this type of gait. This is seen in normal pressure hydrocephalus.

(i) Magnetic gait—with each step the feet may appear glued to the floor. This is seen in myotonia and frontal lobe tumours.

(j) Shuffling gait—it is associated with short shuffling steps and is seen in spasticity.

(k) Festinant gait—it is rare in children and is seen in juvenile onset parkinsonism. The patient walks with rapid, short, stiff and shuffling steps. The associated movements of the arms are absent. He walks with his back bent and appears as if he is trying to catch up with the centre of gravity. If asked to stop, he cannot stop walking immediately.

(l) Functional gait (astasia abasia, variable gait, hysterical gait)—the child appears ataxic and abnormal swaying is present at the hips rather than the ankles. The gait may be inconsistent with rest of neurological examination. The abnormality decreases when the child is not watched or when his attention is diverted by asking him to clap hands while walking. The abnormality in the gait becomes worse when watched. The children with this gait do not fall down or injure themselves.

(m) Hyperkinetic gait—it is seen in chorea and dystonia. In chorea, the distal movements and in dystonia, the proximal movements are marked.

Involuntary Movements

Abnormal involuntary movements are seen in children with lesions in the extrapyramidal system. These are discussed in detail on page 609.

Sensory System

Examination of sensory system requires a great deal of cooperation from the patient. The child should be examined for the following sensations:

1. Superficial sensations—these include touch, superficial pain and temperature.
2. Deep sensations—these include deep pain, pressure, position, vibration and joint sense.
3. Cortical sensations—these include sensations which involve the primary sensory areas of the cortex to perceive the stimulus and the sensory association areas for interpretation. The cortical sensations are as follows:
   - Tactile localisation—ability to localise the stimulus and recognise the spatial relationship. With the child's eyes closed, touch various parts on the body on both sides. See if the child can localise the points correctly.
   - Tactile perception—ability to perceive stimulus and correlate with the memory of past stimulus.
   - Two-point discrimination or spatial discrimination—ability to differentiate cutaneous stimulation at two different points separated by a distance of at least 2 mm.

- Stereognosis—ability to recognise the size, shape, dimensions, texture and form of objects and other relevant information. Astereognosis (stereoanaesthesia) is loss of ability to recognise and identify objects by touch despite intact primary sensations.
- Graphesthesia/traced figure discrimination—ability to recognise letters or numbers written on the skin with a blunt pin. The testing can be done over the dorsum of hands, palms, etc. Letters of size of about 1 cm in height are written. Loss of this sensation is known as agraphesthesia.
- Tactile extinction/sensory extinction/inattention (perception rivalry)—inability to perceive two simultaneous stimuli. The body is stimulated at two analogous points at the same time. In contralateral parietal lobe lesions the perception of the sensation on one side (opposite to the side of parietal lobe lesion) is extinguished. The perception of the sensations is normal on both sides when tested separately. In hemiplegia with hemianaesthesia, the patient perceives the stimulus on one side (normal side) only.
- Autotopagnosia/somatotopagnosia/body image agnosia—inability to identify body parts and orient the body or understand the relation of individual parts. The child suffers from complete loss of personal identification of one limb or one side of the body.
- Anosognosia—absence of awareness or denial of the existence of the disease which is seen in the lesions of right parietal lobe.
- Finger agnosia—inability to name or recognise fingers.
- Sensory dissociation—pain and temperature sensation is lost with preservation of touch sensation. This is seen when only lateral spinothalamic tracts are affected.

Examination of Cerebellum

Cerebellum is associated with regulation of tone of muscles on the ipsilateral side of the body. This results in smooth coordinated movements. These are summarised in Table 11.31.

Autonomic System Examination

The autonomic system operates through craniosacral outflow (Table 11.32). It consists of sympathetic and parasympathetic system.

1. *Sympathetic system*: It prepares the body for 'fight and flight'. Stimulation of sympathetic system causes increased sweating, dilated pupils, increased heat rate and increased blood flow to the muscles.
2. *Parasympathetic system:* It helps in maintaining a normal state of the body.

The effects of sympathetic and parasympathetic stimulation on various organs are summarised in Table 11.33.

Examination of Spine and Cranium

The brain and spinal cord are protected by cranium and spine. Hence, any defect in these may be associated with neurological damage.

Spine

- Spinal tenderness
- Spinal deformities—gibbus may be associated with neurological deficits due to spinal cord compression
- Painful movements
- Spinal dysraphism such as meningomyelocele and spina bifida are associated with hydrocephalus
- Tuft of hair is associated with neurocutaneous syndromes (Fig. 11.21)

Cranium

- Size of the skull (microcephaly/macrocephaly)—microcephaly may be associated with cerebral atrophy and increased head circumference with hydrocephalus
- Shape of the skull—dolichocephalic head in Sotos syndrome
- Fontanels (anterior and posterior)—open or closed
- Sutures—prominent in primary microcephaly
- Suture lines (closed or separated)—sutural widening is seen in conditions associated with increased ICT
- Congenital malformations—craniovertebral

TABLE 11.31 Cerebellar Signs

Parts	Signs
General	Hypotonia Ataxia (incoordination of movements) Decompensation of movements
Head and face	Titubation—sideward movement of the head
	Nystagmus in the horizontal plane. The nystagmus is jerky with fast and slow components. The fast component will be in the direction of the cerebellar lesion. The amplitude will be greater and the rate will be slow when the eyes are deviated to the side of lesion
	Speech—the speech may be scanning or staccato. Dysarthria, irregular, slurred, scanning speech where syllables tend to be separated from each other/staccato speech dysarthria is seen due to incoordination of the muscles of articulation
	Slow saccades—saccadic movements slow
Disorders of ocular movement	Ocular bobbing—rapid downwards conjugate deviation of both eyes followed by slow return Opsoclonus—conjugate irregular jerking in all directions Ocular flutter—ocular dysmetria. Eyes overshoot the target and oscillate for a short time before fixing on it Skew deviation—the eye on the side of the lesion is turned inwards and downwards. Contralateral eye is outwards and upwards
Upper limbs	Dysmetria—past pointing—inability to measure the distance and force of movement Finger–nose test/finger–finger–nose test
	Rebound phenomenon—strong contraction against resistance cannot be controlled on the sudden resistance is removed. Ask the patient to flex the upper arm against resistance. Now the resistance is suddenly removed. In normal persons the further flexion will be minimal and the movement stops. In patients with cerebellar lesions or the lesion to its connections, the flexion continues and the patient may hit his face. The examiner should try to avoid the patient's hand hitting his face by placing his other hand between the testing hand and the patient's face
	Intention tremor—combination of dyssynergia and dysmetria is due to irregular tremor which increases as the hand approaches the target. The tremor is exaggerated when the hands approach an object. This can be demonstrated by finger–nose test, finger–finger–nose tests Dyssynergia—movement involving more than one joint will be broken into their component parts. Past pointing while reaching for objects
	Handwriting—macrographia
	Arm drift—ask the child to keep the arm in supination at 90° to the axis of the body. Ask the child to close the eyes. The affected hand will descend down with slow pronation
	Arm bounce—the rebound test is tested by sudden downwards pressure over the expended upper limb. In cerebellar lesion there will be several oscillations before the arm comes to original position
	Dysdiadochokinesia rapidly alternating movements will be clumsy, irregular and jerky
Trunk	Truncal ataxia—difficulty in sitting, standing, etc. (occurs in vermis lesion)
Lower limbs	Heel–knee test
	Walk round the chair—tend to fall when the child walks with the chair on the side of the cerebellar lesion. The patient is asked to walk around a chair. First the patient is asked to walk round the chair, with the unaffected side near the chair. Then ask the patient to walk with the affected side near the chair. The patient will tend to fall, when he walks with the affected side facing the chair
	Pendular knee jerk—the knee jerk will have oscillations of equal frequency
	Tandem walking—cannot walk along a straight line. The patient is asked to walk along a straight line. A normal person can walk without falling. But in cerebellar lesions the patient tends to fall on the side of the lesion
	Stance ataxias—the patient will have a tendency to fall on the side of the cerebellar lesion Ataxic gait—reeling gait/lurching gait

TABLE 11.32 Autonomic System—Craniosacral Outflow

Part of Nervous System	Autonomic Outflow
Cranial nerves	III, VII, IX and X
Thoracolumbar	T_1–L_2 sympathetic
Sacral	S_2–S_4 parasympathetic

TABLE 11.33 Effects of Sympathetic and Parasympathetic Stimulation

Organ	Sympathetic System	Parasympathetic System
Pupil	Dilatation (α)	Constriction
Accommodation	Decreased	Increased
Heart-chronotropic/ inotropic effects (β)	Positive	Negative
Arteries	Vasoconstriction (α) Vasodilatation (β)	Vasodilatation
Veins	Vasoconstriction (α) Vasodilatation (β)	–
Respiratory tract	Broncho dilatation (β)	Bronchoconstriction
Gastrointestinal tract	Motility decreased (β)	Increased motility
Sphincters	Contraction (α)	Relaxation
Bladder detrusor	Relaxation (β)	Contraction
Bladder sphincter	Contraction (α)	Relaxation
Salivary glands	Scant, thick, viscid saliva (α)	Copious, thin, watery saliva
Skin	Piloerection present	Absent
Sweat glands	Increased secretion (cholinergic)	Decreased secretion
Glycogen metabolism	Glycogenolysis and lipolysis (both α and β)	Glycogen synthesis

anomalies, platybasia, atlantoaxial dislocation, occipital encephalocoele (Fig. 11.22)

- Bruit over the skull—observed in children with arteriovenous malformations and berry aneurysms

Signs of Meningeal Irritation

- Neck stiffness—meningeal irritation results in spasm of the extensor muscles of the neck causing resistance to the flexion of the neck (Fig. 11.23).
- Kernig's sign—with the patient in supine position, the examiner should flex the hip and the knee. This is followed by passive extension of the knee. The examiner then tries to straighten the patient's leg slowly and gently. In the presence of meningeal irritation, it is impossible to straighten



FIGURE 11.21 Child with tuft of hair on back.



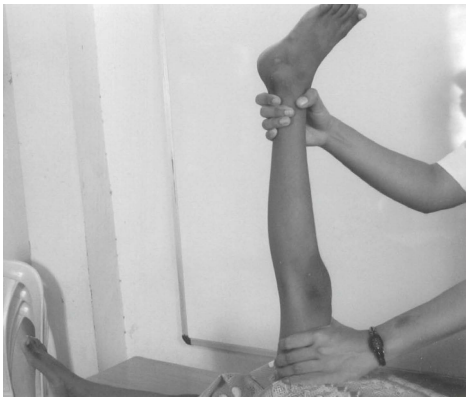
FIGURE 11.22 Child with occipital encephalocoele.



FIGURE 11.23 Testing neck stiffness.



(a)



(b)

FIGURE 11.24 Steps for elicitation of Kernig's sign.



(a)



(b)

FIGURE 11.25 Brudzinski's sign. (a) Neck sign. (b) Leg sign.

the leg because of the painful spasm of hamstring muscles (Fig. 11.24).

- Brudzinski's sign—it has two components. Flexion of neck produces flexion of hips and knees. This is the neck sign. Flexion of one lower limb causes flexion of opposite limb immediately. It is the leg sign (Fig. 11.25).
- Benda's sign—this is of importance in TBM. The sign is elicited by turning the head and chin of the child to one side and observing the shoulder. If there is upwards and forwards movement of the shoulder, the sign is considered positive. It may be positive on one or both sides. This shoulder movement is due to spasm of the trapezius muscle.

Examination for Increased ICT

- Measurement of head circumference
- Examination of fundus for papilloedema by using an ophthalmoscope
- Macewen's sign (crack-pot resonance)—see Chapter 3

Soft Neurological Signs and Symptoms

Soft neurological sign is a deviant performance of a motor or sensory test that is abnormal for a particular age. There is considerable variation in expression of these signs by patients depending on the age, sex and maturation of CNS. These are seen in normal children during the various stages of their neurodevelopment. Absence of these signs at the expected age or presence at an unexpected age is abnormal and should be evaluated.

These signs are usually missed while examining a case with neurological illness.

These signs reflect the abnormalities in the development or maturation of CNS. Series of

timed motor act should be observed. The quality and precision of the patient's movement should be compared with a normal control of similar age and sex.

Significance

A single sign may be observed in normal child. Persistent presence of two or more signs is seen in children with neurological dysfunction—attention deficit disorders, learning or reading disorders, cerebral palsy, etc. These should be observed for future development.

Examination of Peripheral Nervous System

Any lesions in the peripheral nervous system can present with neurological manifestations like weakness and paralysis of muscles. Look for the following features:

- Thickening of nerve
- Neurofibroma
- Tropical ulcers

CLINICAL ASSESSMENT OF THE LEVEL OF LESION

Weakness/paralysis occurs either due to a lesion in cerebral cortex (UMN) or at the level of spinal cord and peripheral nerves (LMN). The differences between UMN and LMN lesions are given in Table 11.34. The level of lesion is determined by the examination of cranial nerves, reflexes and sensory and motor levels. The horizontal level of lesion can be extradural/intradural. If intradural, the examiner should determine whether it is extramedullary or intramedullary. The bladder and bowel involvement should also be determined. The spinal segments and their corresponding vertebral bodies are as follows:

Vertebral body	Corresponding spinal segment
Cervical	Add 1
Thoracic 1–6	Add 2
Thoracic 7–9	Add 3
Thoracic 10	Lumbar 1 and 2
Thoracic 11	Lumbar 3 and 4
Thoracic 12	Lumbar 5
Lumbar 1	Sacral and coccygeal

TABLE 11.34 Differences between UMN and LMN Lesion

Features	UMN Lesion	LMN Lesion
Level of lesion	From cerebral cortex up to cranial nerve nuclei or anterior horn cell (cerebral cortex, midbrain, pons, medulla, spinal cord)	Cranial nerve nuclei or anterior horn cells to motor end plate (cranial nuclei or anterior horn cell, cranial nerves, peripheral nerves)
Distribution of weakness	Weakness is more in antigravity muscles	Consistent with the spinal segments and nerves
Muscles affected	Muscle groups affected	Single muscles affected
Cause of decreased movements	Paralysis of movements	Paralysis of muscles
Tone	Increased Spastic—clasp-knife type	Decreased Flaccid
Muscle wasting	Disuse atrophy	Atrophy and wasting
Power	Weakness less affected than lower motor neuron	Weakness more affected than upper motor neuron
Superficial reflexes	Lost or diminished	Lost
Deep tendon reflexes	Exaggerated	Absent or diminished
Clonus	Present	Absent
Fasciculations	Absent	Present if the anterior horn cells are involved
Plantar reflex	Extensor	Flexor or absent
Reaction of degeneration in the muscles	Absent	Present

EXAMINATION OF OTHER SYSTEMS

Lesion in the nervous system may be associated with pathology in other systems. Also, defective functions of the nervous system have an effect on other systems. Hence, other systems should be examined while examining nervous system.

Cardiovascular System

Cardiovascular disorders may result in thromboembolic manifestations in the nervous system. The examiner should look for congenital heart diseases—both cyanotic and acyanotic. Decreased cardiac output due to cardiac failure predisposes to brain hypoxia and altered level of consciousness. Hypertension predisposes to cerebral haemorrhage.

Respiratory System

Many respiratory disorders predispose to symptoms in the nervous system. Also, some of the neurological disorders present with respiratory symptoms. Hypoxia due to respiratory disease may result in cerebral hypoxia. Respiratory failure may occur due to depression of respiratory centre. Suppurative lung diseases predispose to infections spreading to brain. Koch's lung may be associated with TBM, tuberculoma, tuberculous endarteritis, etc.

Gastrointestinal System

Look for hepatosplenomegaly which is associated with storage disorders such as mucopolysaccharidoses which also infiltrates brain. Dehydration due to gastroenteritis results in haemoconcentration and predisposes to cortical vein thrombosis and brain infarction. This presents as altered sensorium and focal neurological deficits. Shigella encephalopathy may be associated with haemolytic uraemic syndrome.

HEMIPLEGIA

The term hemiplegia indicates paralysis of one side of the body involving the arm and leg, and usually also the face (faciobrachiocrural hemiparesis). The term 'crossed paralysis' or 'crossed hemiplegia' refers to paralysis of ipsilateral cranial musculature with contralateral hemiplegia. It is a sign of brain stem disease.

TABLE 11.35 Anatomical Classification of Hemiplegia

Type	Site of Lesion
Cerebral • Cortical hemiplegia • Subcortical • Capsular hemiplegia (classical)	 Cerebral cortex Corona radiata Internal capsule
Crossed Contralateral hemiplegia	Brain stem with cranial nerve involvement (Weber syndrome, Benedict syndrome)
Cruciate hemiplegia	When the lesion is at the level of decussation of medullary corticospinal fibres, there will be paralysis of arm on one side and the legs on the other side
Cord hemiplegia	Spinal cord (upper cervical and lower cervical)
Carotid hemiplegia or stuttering hemiplegia	Carotid artery (triad of symptoms—visual disturbances, carotid bruits, hemiplegia)

CLASSIFICATION

I. Anatomical classification is based on the site of lesion (Table 11.35)
II. Based on tone
    1. Spastic hemiplegia—tone increased
    2. Flaccid hemiplegia—tone decreased
III. Based on age of onset
    1. Congenital hemiplegia
    2. Infantile hemiplegia
    3. Adult hemiplegia

Differences between infantile hemiplegia and adult hemiplegia are given in Table 11.36.

CAUSES

- Primary—the lesion originates in the CNS. The causes are space-occupying lesion, CNS infection, subarachnoid haemorrhage (stroke).

TABLE 11.36 Differentiating Features between Infantile and Adult Hemiplegia

Features	Infantile Hemiplegia	Adult Hemiplegia
Site of lesion	Cortical/subcortical area	Internal capsule
Convulsions	Common	Uncommon
Speech	Not affected (unaffected side will takeover)	Affected—dysphasia
Mental retardation	Common	Rare
Growth retardation	Shortening of limbs Hemiatrophy	No shortening
Differential involvement	Upper limbs > lower limbs	Upper limbs = lower limbs
Muscle wasting	Present	Absent Disuse atrophy present
Involuntary movements	Less common	Common on the affected side
Plantar reflex	May be flexor	Extensor
Abdominal reflex	Retained, often normal (still a local reflex)	Lost
Sensory—loss of cortical sensations	Common	Not common
Autonomic—vasomotor changes	Warm, erythematous, oedematous limbs	Less common

TABLE 11.37 Causes of Hemiplegia

Primary Causes	Secondary Causes
CNS infection Subarachnoid haemorrhage	Congenital heart diseases Bronchiectasis Haematological causes Malignancy—leukaemia Bleeding disorders—thrombocytopenia

- Secondary—the source of lesion lies outside the CNS. For instance, thrombosis, embolism or haemorrhage in CNS may be a result of some congenital cardiac defect or some haematological disorder. Secondary deposits from malignancies can directly result in neurological deficits (Table 11.37).

TABLE 11.38 Causes of Stroke

Causes	Presentation	
Thrombosis	Sleep and stroke	Usually occurs during sleep and may improve. Marked neurological deficiencies will be seen.
Haemorrhage	Strain and stroke	Will be associated with severe neck pain if there is subarachnoid haemorrhage. It may be associated with hypertension.
Embolism	Sudden stroke	A source of embolism may be found such as infective endocarditis.

STROKE

It refers to rapidly developing loss of brain function(s) due to disturbance in its blood supply. The commonest vessels involved are as follows:

- Charcot artery (artery of haemorrhage)—branch of middle cerebral artery
- Heubner's artery—branch of anterior cerebral artery

Causes

- Thrombosis
- Haemorrhage
- Embolism

Their mode of presentation is discussed in Table 11.38. The differentiating features are given in Table 11.39.

Investigations

- CT scan with contrast
- Four-vessel cerebral angiography

CLINICAL FEATURES

Clinical presentation varies according to the site of lesion.

1. Ipsilateral hemiplegia—the cranial nerve palsy is on the same side as that of hemiplegia. This indicates that the lesion is above the level of

TABLE 11.39 Differences between Thrombosis, Embolism and Haemorrhage

Features	Thrombosis	Embolism	Haemorrhage
Age	Middle age	Young age	Middle age
Onset	Progressive	Instantaneous	Catastrophic
Time of onset	During sleep Immediately after waking up	Precipitated by exertion	When patient is awake
Progression	Stuttering, step ladder	Maximal at onset	Progressive, minutes to hours
Carotid bruit	May be present	May be present	Not present
Hypertension	Mild	Absent	Severe
Heart	Normal	Endocardial or myocardial lesion	Normal
Increased intracranial tension	Absent	Absent	++
Neck stiffness	Absent	Absent	+
Convulsions	Rare	Common	Common
Cerebrospinal fluid	Normal	Normal	Blood stained
Management	Vasodilators, thrombolytics	Anticoagulants	Epsilon aminocaproic acid
Risk factors	Nephrotic syndrome, Dehydration Cyanotic heart disease Polycythaemia	Congenital heart diseases with shunts, Atrial fibrillation Infective endocarditis Atrial myxoma, Air emboli, Septic emboli from abscess	Stress, emotion Rupture of Arteriovenous malformations (berry aneurysms) Coagulopathy Thrombocytopenia Hypertension

brain stem, that is, in the cortex, internal capsule or subcortical region.

2. Contralateral hemiplegia—the cranial nerve palsy is on the side opposite to that of hemiplegia. This indicates that the lesion is below the level of brain stem.

Table 11.40 gives the clinical presentation depending on the artery involved.

INVESTIGATIONS

1. To confirm the cerebrovascular accident—CT scan
2. To find out the aetiology
   - Blood count (leukaemia, polycythaemia)
   - Peripheral smear study
   - Haemoglobin
   - Platelet count (thrombocytopenia)
   - Erythrocyte sedimentation rate—increased in vasculitis
   - Silver prusside reaction for homocystinuria
   - Antinuclear antibody tests (systemic lupus erythematosus)
   - Protein C and S, antithrombin III estimation—hypercoagulable states

TABLE 11.40 Part of the Cerebral Artery Affected and the Clinical Features

Artery Involved	Features
Anterior cerebral artery	Snout reflexes present, Palmomental reflex present Incontinence of urine Cerebral paraplegia in bilateral occlusion Cortical sensory loss Flaccid lower limb and spastic upper limb
Middle cerebral artery	Face and arm more involved Flaccid upper limb and spastic lower limb Posterior branch affected—Wernicke's aphasia Cortical sensory loss
Posterior cerebral artery	Visual defects Loss of colour recognition Loss of memory or name of objects

- Serum lactate/pyruvate—MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke), mitochondrial encephalopathies
- Blood culture—infective endocarditis
- Chest X-ray—may show evidence of tuberculosis and congenital heart defects
- Electrocardiogram—may show changes in presence of congenital heart defects
- Echocardiogram
- Doppler study—carotid artery disease
- Arteriography—arteriovenous malformations
- Cerebrospinal fluid (CSF) analysis—meningitis
- Tests for sickling—sodium metabisulphite added to the smear can precipitate sickling. Cover the smear with a cover slip and coat the sides with wax. This enhances the sickling

3. Neurological work-up
   - Lumbar puncture
   - Electroencephalogram (EEG)
   - X-ray skull
   - Carotid arteriography
   - CT scans
   - MRI
   - Digital subtraction angiography

TREATMENT

1. Supportive
   - Physiotherapy
   - Rehabilitation
   - Prevention of bedsores
2. Symptomatic treatment—it consists of treatment of seizures
3. Treatment of specific conditions
   - Bacterial meningitis should be treated with appropriate antibiotics
   - Tumours should be removed surgically
   - Vascular abnormalities should be corrected surgically
   - Intra-arterial thrombolytics can be given if the child is treated within 12 hours. Heparin and streptokinase can be given in selected cases
   - Antiplatelet agents
   - Source of embolism should be treated
   - Cardiac abnormalities should be corrected
   - Suppurative lung disorders, infective endocarditis should be treated with antibiotics

PROGNOSIS

It depends on the aetiological factors. Multiple or prolonged seizure at the onset is a bad prognostic sign. Complete recovery is unlikely when there is no improvement in the first week of illness.

VARIANTS

Alternating Hemiplegia of Childhood

- Age of onset is before 18 months of age.
- Pathogenesis—this is due to circulatory disturbances in the vertebrobasilar circulation.
- Clinical features—the child presents with repeated bouts of hemiplegia which may be associated with paroxysmal tonic or dystonic attacks, unilateral nystagmus, strabismus and autonomic disturbances. This disappears on going to sleep and recurs in prolonged bouts about 10–20 minutes after waking up.

Sensory Hemiplegia

There is loss of sensation on one side of the body. This is seen in the following conditions:

- Lesion in thalamus (commonest cause)—sensory loss on contralateral side
- Cortical lesion—sensory loss on contralateral side
- Lateral medullary syndrome—sensory loss on the opposite side
- Trigeminal—sensory loss on face on the same side

COMPLICATIONS

- Bedsores
- Contractures

- Convulsive disorders
- Deep vein thrombosis
- Embolisms—pulmonary embolism is common
- Frozen shoulder
- Growth retardation on the affected side (cortical hemiplegia)
- Infections—bronchopneumonia, urinary tract infections (UTIs)
- Joint deformities—fixed flexion deformities

PARAPLEGIA

Paraplegia is a condition where there is complete or incomplete motor weakness or paralysis of both the lower limbs, and possibly the trunk but not the arms. The involvement of trunk depends on the level of spinal cord injury. Paraplegia usually results from spinal cord lesion below the level of T_1.

CLASSIFICATION

I. Based on the extent of injury to spinal cord
   1. Complete paraplegia—complete transection of spinal cord results in complete paralysis below the level
   2. Incomplete paraplegia—it occurs due to partial damage to the spinal cord. Some motor and sensory function remains. The features depend on the area affected (anterior, lateral or posterior). Below the level of lesion, there may be only sensory impairment with no noticeable loss of motor function; or there may be only motor impairment with no noticeable loss of sensory function (touch and pain preserved). Incomplete paralysis with profound weakness may be followed by total paralysis in some children

II. Based on tone
   1. Spastic paraplegia—it is an UMN type of paraplegia and occurs due to lesion in corticospinal tract. The causes are as follows:
      - Infectious disorders (tropical spastic paraplegia)
      - Traumatic—spinal cord transection
      - Congenital developmental disorders—cerebral palsy, Arnold–Chiari syndrome and hereditary spastic paraplegia
      - Degenerative disorders—Devic's disease
      - Hereditary disorders—adrenoleukodystrophy, Schilder's disease, Krabbe's leukodystrophy, Pelizaeus–Merzbacher disease and Sjogren–Larsson syndrome
      - Compressive lesions of spinal cord
      - Poisoning—lathyrism
   2. Flaccid paraplegia—it is an LMN type of paraplegia and occurs due to lesion in anterior horn cells and peripheral nerves

III. Other types
   1. Paraplegia in extension—when only the corticospinal tract is affected, the reticulospinal tract of the extrapyramidal system causes an increased tone in the antigravity muscles. This is called paraplegia in extension
   2. Paraplegia in flexion—when the extrapyramidal system is also affected along with the corticospinal tract, the muscle tone is controlled by the spinal reflex arc. Hence, there is an increased tone in the flexors more than the extensors. This indicates a total loss of control of the spinal cord by the central pathways and indicates a severe injury to the spinal cord. In this condition, withdrawal or flexor reflex (withdrawal of the limbs in response to a stimulus applied to any point in the affected part) is present. Sometimes the stimulus below the affected part leads to a flexor spasm, emptying of bladder and bowel and seminal emission. This is called mass reflex

Differences between paraplegia in extension and flexion are given in Table 11.41.

CAUSES

1. Intracranial—the motor cortical representation for the legs is in the parasagittal region. Hence, any lesion affecting the parasagittal region on

TABLE 11.41 Differences between Paraplegia in Extension and Paraplegia in Flexion

Features	Paraplegia in Extension	Paraplegia in Flexion
Level of lesion	Only pyramidal tracts are involved	Both pyramidal and, extrapyramidal tracts are involved
Clinical features		
Attitude	Hip extended, adducted knee extended	Thigh and knee flexed Feet dorsiflexed
Tone	Increased in extensors	Increased in flexors
Jerks	Brisk	Decreased
Plantar	Extensor	Extensor
Withdrawal reflex	Not present	Present
Mass reflex—stimulus below the lesion results in flexor spasm, emptying of bladder and bowel	Absent	May be present

TABLE 11.42 Differences between Compressive and Non-compressive Causes

Features	Compressive	Non-compressive
Onset	Gradual	Acute
Bladder and bowel involvement	Early	Late
Root pain	Present	Absent
Symmetry	Asymmetrical	Symmetrical
Bony tenderness and deformity	Present	Absent
Upper level of sensory loss	Present	Usually absent but may be present in transverse myelitis
Flexor spasm	Present	Absent
Zone of hyperaesthesia	Present	Usually absent but may be present in transverse myelitis

both sides leads to paraplegia

- Anterior cerebral artery syndrome—thrombosis of unpaired anterior cerebral artery or both the anterior cerebral arteries
- Sagittal sinus thrombosis
- Cerebral palsy
- Brain tumour
- Acute demyelination
- Acute disseminated encephalitis
- Parasagittal meningioma/parafalcine meningioma compresses the medial frontal lobe bilaterally
- Multiple sclerosis (rare in children)

2. Spinal—these may be non-compressive or compressive (Table 11.42)
   (a) Non-compressive
   - Metabolic myelopathy—vitamin B_{12} deficiency
   - Inflammatory myelopathy—acute transverse myelitis, vasculitis, systemic lupus erythematosus, multiple sclerosis
   - Infectious myelopathy—transverse myelitis, herpes zoster myelitis, poliomyelitis, HIV
   - Postinfective demyelination—Guillain-Barré syndrome
   - Vascular myelopathy—spinal cord or cerebral infarct, haematomyelia, anterior spinal artery syndrome
   - Demyelinating disorders—Devic's disease, postinfectious demyelinating myelitis, human T lymphotropic virus (HTLV-1) associated myelopathy
   - Degenerative disorders—hereditary diseases, Friedrich's ataxia, hereditary spastic paraplegia, familial spastic paraplegia, motor neuron disease, syringomyelia
   - Trauma—acute spinal cord injury

   (b) Compressive myelopathy—extradural and intradural (extramedullary/intramedullary) (Tables 11.43 and 11.44)
   - Extradural—spinal epidural abscess or haemorrhage/haematoma, dumbbell tumours, meningioma, vertebral disc prolapse, vertebral dislocation or fracture causing spinal cord compression, Klippel–Feil syndrome, cervical spondylosis, dislocation of spine (spondylolisthesis), vertebral osteoma, spon-

TABLE 11.43 Differences between Extradural and Intradural Lesions

Features	Extradural Lesions	Intradural Lesions
Local pain	Present	Absent
Local tenderness	Present	Absent
Root pain	Present	Absent
Causes	Vertebral tumours, extradural abscess	Glioma, astrocytoma

dylo epimetaphyseal dysplasia with joint laxity, vertebral tumour, caries spine, bony metastasis, multiple myeloma, cauda equine syndrome (compression by central disc herniation)

- Intradural extramedullary—extra-arachnoid (neurofibroma), intra-arachnoid (dermoid cyst, seeding from cerebral tumours, subdural abscess, subdural haemorrhage, arachnoiditis, neurofibroma, meningioma, meningomyelocele)
- Intradural intramedullary—glioma, ependymoma, astrocytoma, haemangioma, haematoma, hydromyelia, syringomyelia

3. Anterior horn cells
   - Motor neuron disease
   - Amyotrophic lateral sclerosis
4. Neuromuscular junctions
   - Myasthenia gravis
   - Eaton–Lambert syndrome
5. Nerves
   - Peripheral neuropathy
   - Polyneuropathy
   - Polyradiculopathy
6. Muscles
   - Myopathies
   - Polymyositis
7. Miscellaneous
   - Drugs—pancuronium
   - Periodic paralysis (hypokalaemia or hyperkalaemia)
   - Tick paralysis
   - Conversion disorders
   - Paragonimiases (lung infection paraplegia)

TABLE 11.44 Differences between Extramedullary and Intramedullary Lesions

Features	Extramedullary	Intramedullary Lesions
Symptoms		
Initial presentation	Weakness	Sensory loss
Pain	Early root pain Radiating	Late Burning
Weakness	Asymmetric initially	Symmetrical from the beginning
Paraesthesia	Rare until late	Occur in all stages
Sensory disturbances	Late and ascending	Early and descending
Signs		
Sensory deficit	Brown–Séquard type	Dissociative sensory loss
Motor spasms/spasticity	Common due to irritation	Not common
Lower motor neuron signs	Segmental No fasciculations	Marked, wide spread Fasciculations
Upper motor neuron signs	Early/prominent	Late/minimal
Pyramidal tract	Early	Late
Sphincters—bladder and bowel disturbances	Late	Early
Sacral sparing	Not present	Common
Trophic changes	Not marked	Marked
Muscle atrophy	Not common	Common
Spinal tenderness	May be present	Rare
Spinal fluid changes	Common	Rare

- Idiopathic postinfectious polyneuritis
- Dysbarism

INVESTIGATIONS

- Complete blood count
- X-ray spine
- MRI
- CSF study—cytoalbuminologic dissociation in Guillain–Barré syndrome, protein elevated with decreased glucose in pyogenic meningitis
- Nerve conduction studies for neuropathy and polyradiculopathy

- Electromyogram (EMG) for myopathy
- Serum electrolytes—potassium level decreased or increased
- Serum calcium
- Erythrocyte sedimentation rate
- Vitamin B_{12} and folic acid levels
- Myelography
- Evoked nerve potential
- Antinuclear antibody
- DNA testing
- Genetic studies

TREATMENT

Specific Treatment

- Traumatic spinal cord injury—surgical decompression and stabilisation, high-dose steroids
- Infectious myelopathies—antibiotics
- Guillain–Barré syndrome—plasmapharesis, intravenous immunoglobulins within 2 weeks of onset of symptoms
- Multiple sclerosis—steroids for treatment of acute exacerbations (common in adults)

Supportive Care

- Bladder and bowel care
- Physiotherapy
- Assist devices
- Orthotics
- Wheel chairs
- Prevention of complications—deep vein thrombosis and decubitus ulcers

Surgical Treatment

It is done for paraplegia due to causes such as spinal dysraphism. Modalities of surgical treatment are as follows:

- Surgical decompression
- Surgical stabilisation

Recent Advances

Embryonic stem cell therapy can also be used.

PROGNOSIS

The prognosis depends on the aetiology and the extent of injury to the nervous system. In children with traumatic paraplegia, the recovery is maximum in the first 6 months after the injury. The recovery can occur up to 2–3 years.

QUADRIPLEGIA

It is also known as *tetraplegia* and refers to partial or total loss of use of all four limbs and torso, usually due to spinal involvement between C_1 and C_7 vertebrae. *Quad* is a Latin word which means four; *plegia* is a Greek word which means inability to move. Apart from the paralysis of limbs there is autonomic and sensory dysfunction. Quadriparesis refers to weakness of all the four limbs with the upper limbs involved more than the lower limbs. The weakness may be associated with spasticity or flaccidity. The causes of quadriplegia according to site of lesion are given in Table 11.45.

CLASSIFICATION

I. Depending on the tone

1. Spastic quadriplegia
   (a) Vertebral causes

TABLE 11.45 Causes of Quadriplegia

Parts Involved	Conditions
Cerebral cortex	Cerebral palsy
Cervical cord	Craniovertebral anomalies Cervical cord compression at higher level
Anterior horn cell	Anterior poliomyelitis Motor neuron disease Guillain–Barré syndrome
Peripheral nerves	Peripheral neuropathy
Neuromuscular junction	Myasthenia gravis
Muscles	Myopathy
Metabolic and electrolyte disturbances	Periodic paralysis

- Infections—tuberculosis, staphylococcal infections
- Trauma—fractures, dislocations
- Disc prolapse
- Anomalies—craniovertebral anomalies, kyphoscoliosis

(b) Intravertebral causes

- Extradural—epidural abscess, pachymeningitis, leukaemia, lymphoma, tumour (ganglioneuroma, neuroblastoma)
- Intradural—neurofibroma, dermoid cyst, seeding from cerebral tumours, subdural abscess, arachnoiditis, tumours (neurofibroma, meningioma, meningomyelocele)
- Intramedullary—glioma, ependymoma, astrocytoma, haemangioma, haematoma, hydromyelia

2. Flaccid quadriplegia
   (a) Acute inflammatory demyelinating polyneuropathy
   (b) Spinal shock
   (c) Acute poliomyelitis
   (d) Spinomuscular atrophy
   (e) Hereditary motor sensory neuropathy

LEVEL OF LESION

Severity of quadriplegia depends on the level and extent of injury.

1. High cervical cord lesions (C_4 and higher)—when the lesion is at a higher level above C_3, there will be respiratory paralysis due to diaphragmatic paralysis (supplied by phrenic nerve [C_3–C_5]). These lesions can be extramedullary or intramedullary (Table 11.44)
   (a) Extramedullary lesions
   - Atlantoaxial dislocation
   - Fracture dislocation of upper cervical vertebra
   - Cervical spondylosis
   - Tumours

   (b) Intramedullary lesions
   - Cervical cord tumours
   - Haematomyelia
   - Syringomyelia

2. Low level quadriplegia (C_5–C_7)—depending on the level between C_5 and C_7, the quadriplegia may present with following features:
   (a) C_5—shoulder and biceps weakness. Movements at wrist are normal
   (b) C_6—weakness of wrist with normal hand functions
   (c) C_7 and T_1—can straighten the arm but have dexterity problems with hands and fingers

EXTENT OF INJURY

Depending on the extent of injury of spinal cord, the quadriplegia could be complete or incomplete.

1. Complete quadriplegia—complete transaction results in complete paralysis below the level of lesion.
2. Incomplete quadriplegia—it occurs due to partial damage to the spinal cord. Some motor and sensory function remains. The clinical features depend on the area affected (anterior, lateral or posterior part of spinal cord) (Table 11.46).

TABLE 11.46 Features of Incomplete Quadriplegia

Type	Clinical Features
Anterior cord syndrome	Impairment or loss of ability to sense pain, temperature and touch sensations below the level of lesion. Pressure and joint sensation may be preserved.
Central cord syndrome	Damage to the central part of the spinal cord results in loss of function of arms but the functions of the legs may be preserved. Also, the functions of the bladder and bowel will be preserved. The recovery will start in the legs and progress upwards.
Posterior cord syndrome	Difficulty in coordination of limbs. Muscle power will be normal along with normal pain and temperature sensation.
Brown–Sequard syndrome	Damage to one side of the spinal cord results in impaired movements on the side of injury with loss of pain and temperature sensation on the opposite side.

CLINICAL FEATURES

- Horner's syndrome
- Spinal accessory nerve involvement
- Paralysis of sternomastoid and trapezius
- Injury to spinal tract of trigeminal nerve
- Vertical nystagmus
- Mirror image movements

PATTERNS OF PRESENTATION

1. Quadriparesis with UMN signs and posterior column involvement
   - Friedreich's ataxia
   - Subacute combine degeneration
   - High cord lesions
   - Multiple sclerosis is rare in children
2. Quadriparesis with pure LMN signs
   - Guillain–Barré syndrome—polyneuropathy
   - Porphyria—polyneuropathy
   - Poliomyelitis
   - Muscular dystrophy
   - Myasthenia gravis
   - Motor neuron disease
3. Quadriparesis with pure UMN signs
   - Cord compression
   - Cerebral palsy
4. Quadriparesis with both UMN and LMN symptoms
   - With sensory loss—transverse myelitis, myelopathy with radiculopathy, cord lesions
   - Without sensory loss—amyotrophic lateral sclerosis, atypical cord compression
5. Quadriparesis with hypertension
   - Neuropathy due to porphyria, lead poisoning, polyarteritis nodosa, Guillain–Barré syndrome, uraemia, diabetes
   - Bulbar polio
6. Quadriparesis with dementia
   - Cerebral palsy (severe form)
   - Spinocerebellar degeneration
   - Subacute combined degeneration
7. Recurrent quadriparesis
   - Arteriovenous malformations
   - Craniovertebral anomaly (atlantoaxial dislocation)
   - Myasthenia gravis
   - Familial periodic paralysis (hypokalaemia/hyperkalaemia)
   - Guillain–Barré syndrome
   - Hysterical
8. Episodic paralysis
   - Myasthenia gravis
   - Hyperthyroidism
   - Periodic paralysis (hyperkalaemia or hypokalaemia)
   - Guillain-Barré syndrome
   - Primary hyperaldosteronism (associated with hypokalaemia)

CRANIOVERTEBRAL ANOMALIES AND QUADRIPLEGIA

The following craniovertebral anomalies are associated with quadriplegia:

- Atlantoaxial dislocation
- Arnold–Chiari malformation
- Klippel–Feil anomaly
- Hypoplastic odontoid process
- Occipitalisation of atlas
- Platybasia

The presence of Feil's triad may be associated with craniovertebral anomalies. It consists of the following features:

- Short neck
- Restricted cervical movements
- Low posterior hairline

Other features that may be present in a case of quadriparesis associated with craniovertebral anomalies are as follows:

- Cerebellar signs
- Deep tendon reflexes—brisk in all the four limbs
- Gradual onset, usually
- Hypertonia of all the four limbs
- Impaired position and vibration sense
- Wasting of small muscles of hand

INVESTIGATIONS

- X-ray skull
- CT scan
- MRI

TREATMENT

This includes treatment of primary cause by removal of tumour, decompression surgery and treatment of infections, in addition to supportive care. Treatment of quadriplegia depends on the level of lesion.

1. C_1–C_4 lesions—these children require help for personal care and turning in bed. Devices that can be used are as follows:
   - Powered wheel chairs
   - Head rests and troughs
   - Bed surfaces with two or more segments that are alternately inflated and deflated can be used for children who cannot turn in bed
   - Functional electric stimulation helps restore elbow flexion in patients with C_4 lesion
   - Balanced forearm orthosis
   - Long opponens orthosis
2. C_1 and C_2 lesions—these children have normal functional phrenic nerves. Implanted phrenic pace makers are helpful
3. C_3 lesions—children with C_3 lesions have impaired breathing. They require respiratory support. As they can shrug their shoulders, powered wheel chairs can be used. They can use equipment which can be controlled by mouth, head, eyebrows movements or by voice control
4. C_4 lesions—children with C_4 lesions do not need ventilatory support. Rewiring neurological connections may be helpful in regaining slight movements as in the case of an actor by name Christopher Reeve

Supportive Care

- Respiratory support
- Nutritional care—adequate nutritional supplementation
- Prevention of bedsores—frequent turning of the patient, keeping the pressure areas dry, pressure relieving mattress
- Chest physiotherapy—respiratory exercises
- Release of pressure—decompression surgery
- Decreasing the muscle spasticity using drugs
- Maintenance of temperature
- Psychological therapy to prevent depression
- Counselling
- Rehabilitation
- Prevention of clots—physiotherapy, special inflatable pumps placed over the legs to improve circulation
- Prevention of further injury (second trauma)

Treatment of Complications

- Antibiotics for lung infections and UTIs
- Bedsore wound care including debridement
- Special mattresses (ripple mattress, waterbed, etc.)

PROGNOSIS

Recovery is maximum in the first 6 months after injury but may be seen up to 2–3 years. Lifespan is decreased due to complications. Potential for return of functions depends on the following factors:

- Physiotherapy
- Occupational therapy
- Mental attitude of the patients
- General health

CEREBRAL PALSY

Cerebral palsy is a non-progressive disorder of posture and movement often associated with epilepsy and abnormalities of speech, vision and intellect. It results from a defect or lesion of the developing brain.

CLASSIFICATION

I. Anatomical or topographic classification—this classification is based on the extent of involvement of the limbs.

1. Monoplegia—only one limb is paralysed

2. Paraplegia—both the lower limbs are involved in the paralysis
3. Hemiplegia—both upper and lower limbs are involved on one side
4. Tetraplegia or quadriplegia—all the four limbs are involved
5. Diplegia—all the four limbs are involved; lower limbs are more involved than the upper limbs
6. Double hemiplegia—all the four limbs are involved; upper limbs are involved more than the lower limbs
7. Triplegia—three limbs are involved

II. Physiological classification

1. Spastic type of cerebral palsy (70%–80% cases)
   - Diplegia
   - Quadriplegia
   - Double hemiplegia
   - Hemiplegia
   - Paraplegia
   - Triplegia
   - Monoplegia
2. Cerebral palsy with choreoathetoid type of movements (10%–15% cases)
3. Ataxic cerebral palsy (5% cases)
4. Rigid cerebral palsy
5. Atonic cerebral palsy
6. Hypotonic cerebral palsy
7. Dystonic cerebral palsy
8. Athetoid (dyskinetic) cerebral palsy
9. Ballismic cerebral palsy
10. Cerebral palsy associated with tremors
11. Mixed cerebral palsy
12. Unclassified cerebral palsy

III. Functional classification—it is based on the extent of activity that is possible in a child with cerebral palsy (Table 11.47). It helps in planning treatment and rehabilitation.

TABLE 11.47 Grades of Cerebral Palsy

Grade	Extent of Activity	Support Required or Not
I	No limitation of activity	Does not require support for activity
II	Slight to moderate limitation of activity	Requires support for complex activity
III	Moderate to severe limitation of activity	Requires support for day-to-day activities
IV	No purposeful physical activity	Bedridden—totally dependent for all activities

TABLE 11.48 Classification Based on Site of Lesions

Site of Lesion	Type of Cerebral Palsy	Other Features
Cerebral cortex	Spastic	Cortical functions affected
Subcortical white matter	Spastic	Cortical functions not affected
Periventricular white matter	Infantile diplegia	Intelligence normal
Basal ganglia	Athetoid, dyskinetic	Intelligence normal
Cerebellum	Ataxic	Cerebellar signs present
Brain stem	Spastic	Cranial nerves affected
Global lesion	Quadriplegia	Mental retardation

Classification Based on Site of Lesions

The type of cerebral palsy depends on the site of brain involved as shown in the Table 11.48. When the cerebral cortex or corticospinal fibres are involved, spastic cerebral palsy is seen. When the basal ganglia are affected, cerebral palsy with extrapyramidal features such as athetoid or dystonic features is seen. When cerebellum is affected ataxic cerebral palsy is seen. In preterm babies, the cortex is not developed in periventricular region. Hence, the leg fibres that cross in the pyramidal tract are affected. This results in infantile diplegia.

CAUSES

Cerebral palsy may have a prenatal, natal or a postnatal cause.

Prenatal Causes

- Infection
- Hypoxia (placental insufficiency, eclampsia)

- Metabolic
- Toxic
- Genetic–chromosomal anomalies
- Cerebral infarction
- Drugs—teratogenic
- Anomalies of brain

Natal Causes

- Hypoxia
- Birth trauma
- Low birth weight and prematurity

Postnatal Causes

- Infections
- Toxins
- Trauma
- Metabolic—hypoglycaemia, hyperbilirubinaemia

INCIDENCE IN CHILDREN WITH BIRTH ASPHYXIA

All the cerebral palsy cases do not have a history of birth asphyxia and all the cases with birth asphyxia do not have cerebral palsy. Only 8%–10% of cases with cerebral palsy have a history of birth asphyxia. Hence, various other factors are suspected to cause cerebral palsy. There is an apparent increase in the incidence of cerebral palsy in premature and low-birth-weight babies due to improved survival rate, early identification and appropriate interventions. With effective management of the neonatal jaundice with phototherapy, drugs such as phenobarbitone, blood transfusion, etc., the incidence of choreoathetoid type of cerebral palsy has come down.

PATHOLOGY

Cerebral palsy is caused by an insult to the immature brain, any time before birth up to the postnatal period. A single causative factor (anoxia) may result in different pathologic responses by brain. Sometimes, different aetiologic factors result in similar pathologic responses. The following pathological changes can be seen in a child with cerebral palsy:

- Malformations—hypogenesis and dysgenesis
- Infarction, focal necrosis and selective neuronal necrosis in brain stem or cerebral cortex
- Periventricular leukomalacia, necrosis and cystic degeneration of central white matter
- Degeneration and gliosis of hypothalamus, globus pallidus, substantia nigra, cerebral white matter and body of corpus callosum
- Status marmoratus in caudate nucleus, putamen and thalamus
- Non-infarctive telencephalic leukomalacia
- Infective encephalitis/vasculitis—focal and multi-focal encephalitis can lead to porencephaly

CLINICAL FEATURES

- Delayed motor and mental milestones
- Abnormal reflexes—persistence of primitive reflexes (such as Moro, asymmetric tonic neck, palmar grasp and placing reflexes), failure to develop maturational/postural responses (such as traction, Landau, parachute, head righting and trunk righting reflexes) (Fig. 11.26)
- Abnormal muscle tone (hypotonic/hypertonic) (Fig. 11.27)
- Abnormal movements/seizures
- Definite hand preference before 1 year (hemiplegia)
- Skeletal deformities and joint contractures (secondary to spastic muscles)

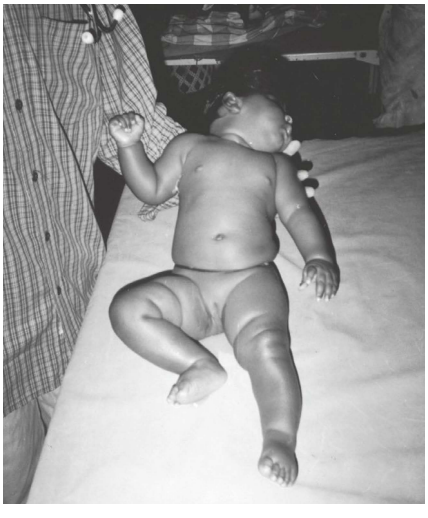


FIGURE 11.26 Asymmetric tonic neck reflex.

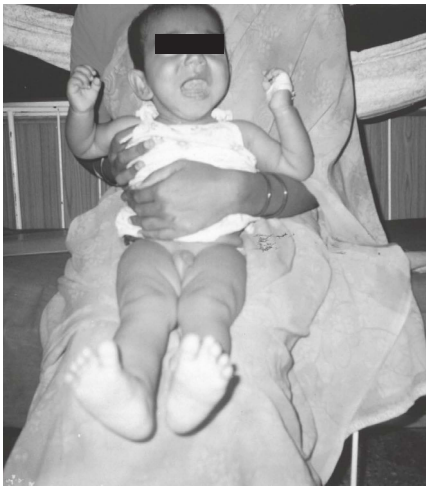


FIGURE 11.27 Hypertonia of lower limbs in a child with cerebral palsy.

- Growth disturbances
- Gait abnormalities
- Problems with posture, balance, coordination, walking, speech, hearing, vision, swallowing, bowel and bladder, etc.

Associated Problems

- Behavioural problems—attention deficit, stubborn, aggressiveness, hyperkinetic behaviour
- Mental retardation
- Epilepsy (grandmal, focal, myoclonus)—in 20% of cases
- Speech disorders—in 50% of cases
- Microcephaly—in 5% of cases
- Hearing problems—sensorineural deafness in athetoid type
- Ocular defects—refractory errors, strabismus, amblyopia, homonymous hemianopia, nystagmus
- Sensory impairment
- Failure to thrive; growth failure
- Skeletal deformities and joint contractures

Abnormal Reflexes

The reflexes which are normally present in the newborn period are inhibited by the developing cortex as the child grows. These are replaced by postural/maturational reflexes. The primitive reflexes are released and can be elicited in a child with cerebral palsy. Examination of these (primitive and protective postural reflexes) is important while examining a child with cerebral palsy. Asymmetry/abnormal persistence of primitive reflexes or failure of protective postural reflexes to develop in a timely manner warrants thorough neurological evaluation for abnormal motor development. The age at which these reflexes normally appear and disappear are given in Table 11.49.

TABLE 11.49 Time of Appearance and Disappearance of Reflexes

Reflex	Age at Which Reflex Usually Appears	Age at Which Reflex Normally Disappears
Primitive reflexes		
Moro	Birth	2–3 months
Stepping	Birth	6 weeks
Placing	Birth	6 weeks
Asymmetric tonic neck reflex	1 month	3–5 months
Crossed extensor reflex	Few days after birth	1 month
Symmetrical tonic neck reflex	2 months	6 months
Sucking and rooting	Birth	4 months—awake 7 months—sleep
Palmar grasp	Birth	6 months
Plantar grasp	Birth	10 months
Adductor response of knee jerk	Birth	7 months
Postural/maturational reflexes		
Neck righting	4–6 months	24 months
Landau	3 months	24 months
Parachute	9 months	Persists for life

DIAGNOSIS

Clinical diagnosis of cerebral palsy should include the following factors:

- Physiologic type—spastic, atonic, ataxic
- Neurological deficits—hemiplegia, quadriplegia
- Mental retardation
- Seizures

- Special senses (hearing, vision)—present or not
- Functional classification—Grade I, II, III, IV
- Microcephaly, if present
- Squint, if present
- Involuntary movements—tremors, athetosis
- Complications—bony deformities and bedsores

INVESTIGATIONS

These are done to rule out other causes of delayed milestones

- Urine screening tests to rule out inborn errors of metabolism
- CSF analysis
- X-ray skull—intracranial calcification
- X-ray spine
- TORCH screening
- EMG
- EEG
- Ultrasonogram of cranium (if anterior fontanel is open) for intracranial haemorrhage
- CT scan
- MRI
- Nerve biopsy
- Myelogram

SPECIFIC TYPES

Spastic Cerebral Palsy

It is the most common type of cerebral palsy and occurs in 70%–80% of all cerebral palsy cases. More than 50% of these patients are of low birth weight. Intelligence is normal or borderline. Apraxia is common. Causes include perinatal hypoxia and kernicterus. There is selective neuronal necrosis in the cortical and subcortical areas. The early and late markers of spastic cerebral palsy are given in Box 11.3. Windswept deformities are common—abduction and external rotation of one hip with the opposite hip in adduction and internal rotation. Other important features include hip dislocation, pelvic tilt, scoliosis and rib deformities, muscle shortening, dystonic posture, abnormal limb growth and contractures. Associated clinical features are as follows:

- Feeding difficulty—due to pseudobulbar palsy which is due to involvement of corticospinal tracts bilaterally
- Constipation
- Reflux oesophagitis

Differential Diagnosis

- Leukodystrophy
- Krabbe's disease
- Infantile Gaucher's disease
- Tay–Sachs disease

Ataxic Cerebral Palsy

The site of lesion is cerebellum and the adjacent brain stem.

Clinical Features

- Hypotonia in all four limbs
- Intellectual impairment
- Intention tremors
- Reflexes—decreased/absent
- Gait—wide-based gait
- Cerebellar signs—gross incoordination, impaired writing skills, dysmetria (lack of ability to judge distances correctly), hypotonia, ataxic gait. Nystagmus is rare.

Differential Diagnosis

- Hereditary ataxia
- Ataxia telangiectasia
- Friedreich's ataxia
- Wilson's disease
- Hydrocephalus
- Congenital cerebellar ataxia
- Posterior cerebellar tumour

Dyskinetic (Extrapyramidal) Cerebral Palsy

This type is characterised by abnormal involuntary extrapyramidal movement patterns along with abnormal tone, posture control and coordination. Child is hypotonic at birth. Abnormal movement patterns (chorea, athetosis, choreoathetosis, dystonia) emerge between 1 and 3 years. The arms are usually more involved than legs. Abnormal movements increase with stress and disappear during sleep. Predisposing factors are perinatal hypoxia and

BOX 11.3 Markers of spastic CP

Early signs

- Ankle clonus
- Absence of pincer grasp
- Asymmetrical reflexes—Moro, parachute
- Asymmetrical fisting
- Brisk reflexes
- Cortical thumb—the thumb will be kept adducted along with fisting
- Absence of Cortical sensations—astereognosis, agraphesthesia
- Convulsions
- Difficulty in manipulation of the affected hand
- Delayed walking—sit and crawl at normal age
- Extension of lower extremity spasticity of ankle resulting in equinovarus deformity
- Fine finger movements are lost
- Fisting of hands
- Fine motor activity affected
- Growth retardation—parietal lobe affected
- Grasp reflex retained
- Gait—circumductory
- Hand preference—early, less than 12 months of age
- Hypotonia progresses to hypertonia
- Homonymous hemianopia
- Increased tone
- Jerk—brisk
- Kinesthesia—paucity of movements on the affected side
- Loss of normal swinging of arms while walking/running
- Moro asymmetric
- Mental retardation
- Newborn reflexes
- One side of the body is affected
- Parachute reflex—asymmetric
- Posture—hypertonia of upper limbs resulting in flexion of elbow joint and metacarpal joints and extension of interphalangeal joints of the upper limb
- Paucity of movements
- Intelligence quotient—decreased
- Reflexes—exaggerated
- Reflexes intact—cremasteric and abdominal
- Spasticity
- Tone increased
- Upper motor signs
- Upper limb affected first
- Visual field defects

Late signs

- Skeletal deformities
- Contractures—arm is adducted, flexed and internally rotated, at the shoulder; elbow is flexed; forearm is pronated; wrist is flexed and thumb is adducted. Leg is adducted and semiflexed at knee with plantar flexion at ankle

kernicterus. Phases in the development of dyskinetic cerebral palsy are as follows:

- Hypotonic phase—at birth
- Dystonic phase—by 4 months of life; no head control, persistence of primitive reflexes, mass movements, sluggish tendon jerks
- Stage of involuntary movements—1–3 years

Clinical Features

- Asymmetric tonic reflex is prominent
- Athetosis appears after 1 year of age
- Bulging fontanels
- Choreoathetosis
- Drooling of saliva
- Deafness—sensorineural hearing loss
- Extensor thrust present
- Extrapyramidal system involved
- Feeding difficulties
- Grimacing of face exaggerated with intention and emotion
- Greenish discolouration of teeth enamel
- Hypotonic (in early stage)
- Head lag
- Involuntary movements—extensor thrust present, choreoathetosis
- Irritability in neonate
- Jerks sluggish
- Lethargy
- Motor disability—severe
- No spontaneous movements
- Nerves (cranial) not involved
- Opisthotonus—may be seen later
- Postural reflexes appear late
- Intelligence quotient (IQ)—preserved
- Reflexes—asymmetric tonic reflex is persistent
- Speech—slow and monotonous
- Skilled hand movements—impaired

- Tongue thrusting problem; prevents food intake
- Tone of muscle normal at rest—may be increased while handling the baby
- Upwards gaze paralysis

Hypotonic or Atonic Cerebral Palsy

It is rare. Lesion may be in frontal lobe and basal ganglia. The injury occurs in early gestational period or soon after birth due to asphyxia neonatorum. Atonic cerebral palsy can be seen in the evolving stage of dyskinetic cerebral palsy and spastic cerebral palsy. The characteristic features are as follows:

- Hypotonia may be generalised or limited to lower limbs
- Hyperreflexia—DTR exaggerated
- Severe mental defect
- Forester's sign—lift the child by holding the axilla. There will be flexion of hips. Later they will develop dystonia or spasticity.

Differential Diagnosis

- Muscular dystrophy
- Werdnig–Hoffman syndrome (atonic diplegia)

Dystonic Cerebral Palsy

- Abnormalities of posture and movement
- Trunk and proximal limbs are affected
- Slow and persistent movement
- Abnormal movements involving head and neck

Mixed Cerebral Palsy

It may present with both pyramidal and extrapyramidal types. Features such as spasticity and choreoathetosis often coexist along with ataxic movements.

MANAGEMENT

Screening and Assessment

Children with risk factors should be screened for cerebral palsy by assessment of developmental milestones. One should look for early pointers for cerebral palsy in such children (Box 11.4). Each child should be assessed clinically and investigations should be done to rule out differential diagnosis. Cases should be picked at the earliest so that structured planning for management and parental counselling can be done.

BOX 11.4 Pointers for diagnosis of cerebral palsy

- Delayed milestones
- Failure to develop protective reflexes (parachute by 9 months)
- Changes in tone and posture
- Psychomotor retardation
- Persistence of primitive reflexes
- Presence of pathological reflexes
- Posture abnormalities—changes in tone and posture
- Progression of illness not present
- Perinatal insult to growing brain

Visual Assessment

- <3 years—miniature toy test
- 3–5 years—illiterate E test
- 6 years—Snellen chart
- Cover test—to detect strabismus

Hearing Assessment

- Auditory brain evoked response (ABER)—neonates
- Behaviour observation audiometry—less than 5 months
- Visual reinforcement audiometry—6 months–2 years
- Play audiometry—2–5 years
- Audiometry—>3 years

Mental Assessment

- Bayley's scale of infant development screening
- Weschler intelligence scale
- Stanford–Binet intelligence scale
- Denver development screening test
- IQ/DQ tests—the IQ testing for children have some drawbacks. One is that most of the children have a scattered pattern of development, that is, they are advanced in some areas and delayed in some areas. Other drawback is that the estimated IQ may be falsely low because of attention deficit disorders

Investigations

1. To rule out other disorders
   - Urine screening tests— to rule out phenylketonuria
   - TORCH, VDRL (Venereal Disease Research Laboratory) tests, ultrasonogram, urine for cytomegalovirus—to rule out intrauterine infections
   - EEG—done to look for epileptic potentials, helps in identifying associated seizures. It also helps in diagnosing progressive degenerative disorders
   - CT scan of brain—detects major congenital anomalies, cerebral atrophy, porencephaly, hydranencephaly
   - MRI—detects neuromigrational disorders such as lissencephaly and schizencephaly, anatomical defects (such as agenesis of corpus callosum), periventricular leukomalacia and lesions in basal ganglia and brain stem
   - Nerve biopsy
   - X-ray spine—to rule out spinal causes of paraplegia
   - X-ray skull—calcification can be seen in intrauterine infections such as toxoplasmosis and cytomegalovirus. In toxoplasmosis, there is diffuse calcification. In cytomegalovirus there is calcification in the periventricular area
   - Myelogram
   - Genetic evaluation—chromosome analysis
   - Metabolic work-up—to rule out inborn errors of metabolism. This includes estimation of organic acids and aminoacid levels, acid base status, ammonia levels, lactic acid levels, endocrine assessment (thyroid function test), calcium and phosphate levels, renal and liver function tests
   - EMG
2. Diagnostic tests
   - Hip radiographs—hip subluxation, maldevelopment of acetabulum
   - MRI scan/CT scan brain—these help in early diagnosis of cerebral palsy. This reveals delayed myelination, thereby helping to suspect cerebral palsy during early infancy. This is not useful after 3 years of age. It is also useful in predicting the outcome in conditions such as infantile diplegia, where the severity of periventricular leukomalacia correlates with the degree of ambulatory problems
   - Gait analysis—it is done by using video cameras and helps in identifying the muscles to be released or lengthened
   - EMG

Treatment

Aim of treatment is not a cure but to alleviate the disability, prevent deformities, achieve maximum possible functions in terms of communication, mobility, independence, education and to lead a near-normal life. It is a multidisciplinary approach. The team consists of paediatrician, paediatric neurologist, physiotherapist, speech therapist, occupational therapist, psychologist, teacher, ophthalmologist, audiologist, ENT surgeon, neurosurgeon, orthopaedic surgeon and a social worker. Parents are important members of this group. The paediatrician is the coordinator of the team. The child is assessed for its capabilities and disabilities. Motor, mental, speech, vision, hearing and psychological disabilities should be assessed. The development quotient or the intelligence quotient should be evaluated. The following lines of management should be followed:

1. Young infant stimulation programme (Table 11.50)—early stimulation programmes are useful in infants under 6 months of age and lead to dendritic and synaptic proliferation. Lack of stimulation results in neuronal extinction
2. Behaviour modification

TABLE 11.50 Various Types of Stimulation of the Cerebral Palsied Child

Type of Stimulation	Stimulus
Vision stimulation	Hold a toy
Hearing stimulation	Talk, sing, play music
Tactile stimulation	Touch the baby
Sensory stimulation	Rub the body and scalp gently
Speech stimulation	Talk to the child

3. Treatment of comorbid conditions—convulsions and reduction of spasm by pharmacotherapy (Table 11.51)
4. Development activation and disability limitation
5. Early intervention—physiotherapy and positioning programmes are needed to prevent sequelae such as contractures
6. Appropriate school placement
7. Appropriate training for self-employment
8. Correction of associated defects
   - Refractory errors—correct with proper lens
   - Squint—corrective surgery
   - Hearing loss—hearing aids

Rehabilitation

1. Parental counselling—aims to help the parents to cope up with the psychosocial stress.
2. Social awareness—this aims to make the child as independent as possible.
3. Counselling for the cerebral palsied children—some children with cerebral palsy with near normal IQ or normal IQ may feel discriminated and rejected. These children need psychiatric intervention.
4. Vocational support.

TABLE 11.51 Drugs Used in Treatment of Conditions Associated with Cerebral Palsy

Conditions	Drugs Used
Abnormal posture	Antispasmodic medications Benzodiazepines (diazepam, nitrazepam) Baclofen (a GABA-receptor agonist) botulinum toxin Dantrolene sodium
Behavioural problems	Tranquillisers
Constipation	Laxatives
Dystonia	Levodopa Carbamazepine Trihexylphenidate
Excessive salivation	Atropine
Seizures	Anticonvulsants
Gait abnormalities	Surgery
Hyperkinetic behaviour	Methylphenidate
Involuntary movements	Haloperidol Sodium valproate Benzodiazepines Tetrabenazine

PROGNOSIS

Good prognostic factors are as follows:

- Infantile cerebral palsy
- Spastic diplegia
- Early intervention
- Good family support
- Absence of associated problems

Bad prognostic factors are as follows:

- Hypotonic cerebral palsy
- Quadriplegia
- Not sitting >4 years
- Not walking >7 years
- Persistent primitive reflexes >2 years

ACUTE FLACCID PARALYSIS

Acute flaccid paralysis (AFP) is defined as onset of paralysis (<4 weeks) in a child (age <15 years) for which no obvious cause has been found; or, paralysis in a person of any age in whom polio is suspected. The paralysis is associated with loss of muscle tone and loss of reflexes. The affected muscles are flabby. Common causes of AFP are as follows:

- Poliomyelitis
- Guillain–Barré syndrome
- Transverse myelitis
- Traumatic neuritis

Their salient features are given in Table 11.52.

Other conditions causing flaccid paralysis are as follows:

- Periodic paralysis
- Polymyositis
- Spinal cord tumours
- Diphtheria
- Porphyria
- Lead poisoning
- Botulism
- Myasthenia gravis
- Spinal shock (spinal cord injury)

TABLE 11.52 Salient Features of Various Conditions Causing Acute Flaccid Paralysis

Disease	Features	Type of Paralysis
Guillain–Barré syndrome	Ascending paralysis Predominantly motor involvement Posterior column signs present	Symmetrical
Transverse myelitis	Pyramidal signs present Sensory involvement Bladder involved	Symmetrical
Poliomyelitis	Pure motor involvement No sensory involvement	Asymmetrical
Traumatic neuritis	Sensory loss	Asymmetrical

LANDRY–GUILLAIN–BARRÉ SYNDROME

It is also known as acute inflammatory demyelinating polyradiculoneuropathy. It is an acute diffuse postinfective disease causing generalised paralysis and areflexia. The disease involves spinal roots, peripheral nerves and occasionally cranial nerves. Amongst the cranial nerves, the VII nerve is most commonly involved. There is immunological reaction due to hypersensitivity that is directed against the myelin sheath of the peripheral nerves. Postinfectious demyelination occurs mainly in motor nerves but sometimes sensory nerves and autonomic nerves are also involved. The disease is not hereditary and affects all the ages.

Predisposing Factors

1. Infections
   - Viral infections—Epstein–Barr virus (infectious mononucleosis), measles, mumps, rubella, varicella, cytomegalovirus, influenza, hepatitis B, hepatitis A, HIV
   - Bacterial infections—*Campylobacter jejuni*, brucellosis. Occasionally acute Guillain–Barré syndrome is associated with *Mycoplasma pneumoniae* or campylobacter infection of respiratory system
2. Systemic lupus erythematosus
3. Hodgkin's disease
4. Sarcoidosis
5. Immunosuppression
6. Rabies vaccine

Pathogenesis

Immunological reaction due to hypersensitivity is directed against the myelin sheath of the peripheral nerves. Microscopically, there is endoneural perivascular mononuclear cell infiltration along with multifocal demyelination involving the peripheral nerves. The demyelination proceeds from root to distal intramuscular nerve ending. However, brunt of the attack occurs on anterior root, proximal spinal nerve and lower cranial nerves.

Non-specific viral infection involving upper respiratory or gastrointestinal tract usually occurs 2–4 weeks prior to the onset of neurological manifestations.

Clinical Features

1. Motor weakness—begins in the lower limbs and progressively involves the trunk, upper limbs diaphragm, respiratory, pharyngeal and laryngeal muscles. Later, there is also involvement of lower cranial nerves. This is known as Landry's ascending paralysis (symmetrical ascending LMN type of paralysis).
   - In the limbs, proximal group of muscles are affected more than the distal group.
   - The paralysis progresses gradually over a period of few days to 10 days (maximum 4 weeks). Thereafter it becomes static, followed by recovery.
   - Tendon reflexes are absent (areflexia) or diminished.
   - Pain in the muscles is an early feature and may be severe enough to mimic encephalopathy in children.
2. Higher functions—consciousness is normal.
3. Cranial nerves—bilateral cranial nerve involvement is frequently seen, especially that of VII nerve. Other nerves that can be involved are III–VI and IX–XII nerves. The cranial nerves I, II and VIII are never involved. Unilateral involvement may occur in early disease.

4. Sensory symptoms—there is no objective sensory loss, rather only subjective sensory disturbances such as paraesthesia of the toes may be present. There may be distal impairment of vibration and position sense in some cases.
5. Autonomic nervous system—the ANS involvement may present as labile blood pressure and postural hypotension, episodes of profound bradycardia and urinary retention.
   - Increased sympathetic activity—episodic or sustained hypertension, sinus tachycardia and tachyarrhythmia.
   - Decreased sympathetic activity—orthostatic hypotension and anhidrosis (loss of sweating).
   - Decreased parasympathetic activity—constipation and visual disturbances (iridoplegia).
   - Increased parasympathetic activity—facial flushing and extreme bradycardia.

Rare Manifestations

- Hyponatraemia—pseudopapilloedema
- Higher mental functions decreased due to hypoxia
- Irritable child with flaccid paraplegia
- Paraesthesia occurs in some cases
- Extraocular muscle movement is rarely seen in Miller Fisher syndrome
- Urinary incontinence/retention
- Abrupt onset

Diagnosis

Diagnostic Criteria

- Weakness of both legs that progresses rapidly upwards
- Areflexia
- Maximum level of weakness is reached within 4 weeks of onset of paralysis
- Absence of fever with the onset of paralysis

Other features that strongly support the diagnosis are as follows:

- History of antecedent viral illness
- Bilateral symmetrical weakness
- Absent or mild sensory symptoms such as paraesthesia
- Cranial nerves—bilateral facial nerve involvement
- Autonomic dysfunction
- Recovery begins 4 weeks after the progression of disease

When to Doubt?

- Marked, persistent asymmetric weakness
- Marked, persistent bladder or bowel involvement
- Bowel/bladder involvement at onset
- More than 50 mononuclear cells in CSF
- Presence of polymorphs in CSF
- Sharp sensory level

Investigations

1. CSF analysis
   (a) Normal pressure
   (b) Appearance—xanthochromic (due to elevated proteins)
   (c) Cytoalbuminological dissociation—usually in meningitis, both the cells and the protein are elevated. In Guillain–Barré syndrome, the protein level is highly elevated but the cell count is not increased or only slightly increased. This is called cytoalbuminological dissociation. This is diagnostic of Guillain–Barré syndrome. Rise in protein begins in late first week and maximises by 2–3 weeks
      - Cell count—normal, no pleocytosis
      - Protein—elevated; twice the upper limit of normal

   (d) Glucose—normal
   (e) Culture—sterile. Viral culture rarely isolates specific virus
2. Nerve conduction velocity studies—suggestive of either axonal or demyelinating neuropathy. Axonal neuropathy has a worse prognosis
3. Electromyography—evidence of acute denervation is present
4. Serum creatinine kinase—normal or elevated minimally
5. Sural nerve biopsy may show
   (a) Segmental demyelination
   (b) Focal inflammation
   (c) Wallerian degeneration

6. Abnormal ECG findings—abnormal ST segment depression, QRS widening and arrhythmia
7. Serology—serum for Epstein–Barr virus and cytomegalovirus antibodies, peripheral neuropathy antibody panel

Treatment

1. Supportive care
   (a) Artificial ventilation if there is respiratory paralysis
   (b) Physiotherapy
2. Immunosuppressive drugs—intravenous high-dose pulse methylprednisolone therapy is useful in some cases
3. Intravenous immunoglobulin therapy—intravenous high-dose immunoglobulin is best given within 3–4 days of onset of weakness
   (a) Indications
      - Acute Guillain–Barré syndrome of less than 2 weeks
      - Inability to walk unaided
      - Bulbar weakness
   (b) Dose—0.4 g/kg/day for 5 days or 1 g/kg/day for 2 days
4. Plasmapheresis—patients with rapid progression of the disease are treated with plasma exchange
   (a) Beneficial in acute Guillain–Barré syndrome of less than 2 weeks duration
   (b) Not much beneficial after 3 weeks
   (c) Favourably modifies poor prognostic factors
   (d) 200–250 mL/kg/body weight of plasma is removed on alternate days in 4–6 sittings within a total period of 8–12 days
   (e) Indications
      - Inability to walk unaided
      - Rapid and significant reduction in vital capacity
      - Onset of bulbar paralysis
   (f) Complications
      - Increased risk of cardiovascular complications and marked dysautonomia
      - Increased risk of transferring hepatitis and AIDS
5. Prevention of secondary infections

TRANSVERSE MYELITIS

It is due to demyelination following certain viral illness.

Clinical Features

- Fever is present before the onset of AFP, but rarely during onset
- Characterised by sudden demyelination of spinal cord (mostly thoracic, may be lumbar or cervical) leading to abrupt onset of progressive weakness and sensory disturbance in the lower limbs with maximal weakness within days
- Paralysis is usually symmetrical and occurs in the lower limbs. It is accompanied by profound anaesthesia to all forms of sensation with a sensory level. Arms may be partially paralysed, but this occurrence is not frequent
- Hypotonia
- DTRs—absent early, hyper reflexia late
- Plantar reflex is extensor
- Bladder involvement occurs early

Course of the Disease

The most common sequence of symptoms is flaccidity of legs, followed by loss of control of anal and bladder sphincters. The disease progresses for 2–3 days and then plateaus. Flaccidity usually changes to spasticity after several weeks and areflexia may be replaced by hyperreflexia. This is followed by recovery in milder cases. Diplegia and atrophy persist in severe cases.

Differentiating features between early and late stages of transverse myelitis are given in Table 11.53.

TABLE 11.53 Differences between Early and Late Stages of Transverse Myelitis

Features	Early Stages	Later Stages
Type of paralysis	LMN type Flaccid	UMN type Spastic
Tone	Decreased	Increased
Deep tendon reflexes	Areflexia	Hyperreflexia
Babinski's sign	Negative	Positive

Investigations

1. CSF study
   - Protein—normal or elevated protein
   - Lymphocyte pleocytosis—moderate
2. MRI
   - Demyelination
   - Spinal cord swelling in severe cases

Treatment

1. Supportive therapy
   - Bladder catheterisation
   - Physiotherapy
2. Steroids—high-dose methylprednisolone therapy intravenously followed by oral steroids

TRAUMATIC NEURITIS

It is due to injury to nerves which may result from direct or indirect trauma. Direct injury is due to penetrating injury to the nerve while giving intramuscular injections. Indirect injury is caused by blunt injury which results in disruption of blood supply to the nerve. The onset of AFP in the affected lower limb occurs from 1 hour to 5 days after injection in the gluteal region. The sequence of events is difficult to establish when injections are applied in both gluteus muscles.

Clinical Features

- Acute flaccid paralysis is accompanied by pain in the gluteal region or along the affected leg.
- Knee jerk is present.
- Ankle jerk is absent or diminished.
- Hip and knee strength is normal. The child walks with a foot drop.
- Atrophy may appear 40–60 days later. However, atrophy after traumatic neuritis never reaches the degree seen in polio.
- Difference in calf circumferences usually does not exceed 0.5–1.5 cm.
- Both lower limbs may be affected in children if injections were given on both sides.

POLIOMYELITIS

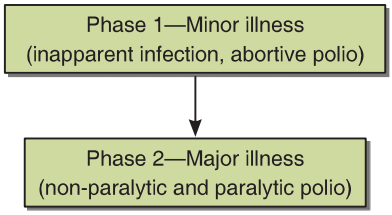
It is one of the most common virus infecting children. It is more common in summer and early autumn in temperate climate. In tropical countries, it may be seen in rainy seasons.

- Infectious agent—the poliovirus belongs to the enterovirus group. It is an RNA virus with three distinct serotypes—type 1 (*Brunhilde*), type 2 (*Lansing*) and type 3 (*Leon*). Type 1 is most frequent and type 2 is least common. Types 1 and 3 cause paralytic polio. The most common type causing epidemic polio is type 1 followed by type 3. Type 2 rarely causes epidemic.
- Reservoir—human beings are the only reservoirs. There is no animal reservoir.
- Mode of transmission—person to person.
- Route of transmission—the virus is transmitted through the faeco-oral route.
- Incubation period—the time from the exposure to the onset of symptoms is 7–14 days, but may range from 4 days to 4 weeks.
- Communicability—the poliovirus is highly communicable. The cases are infective 1 week before and 2 weeks after the onset of paralysis.

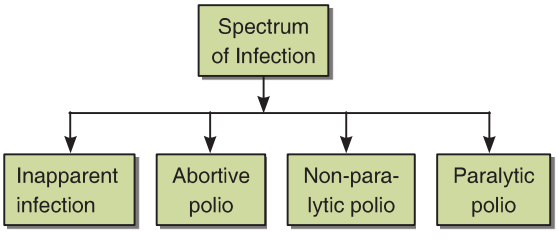
Pathogenesis

The virus multiplies in the intestine when the immunity in the gut declines. After the infection the virus is intermittently excreted in stools for up to 2 months or more. This excretion is maximum just before the paralysis and during the first 2 weeks after the onset of paralysis. From the intestines, the virus travels to the regional lymph nodes and then into the circulation. The virus induces the formation of antibodies in the blood and the gut. If the immune response is good, the infection is aborted. The antibodies act at the site of extraneural proliferation of the virus. The virus infects the nervous system via nerves or blood stream.

The earliest manifestations are associated with the phase of viraemia and consist of fever, headache, sore throat and malaise lasting for 1–5 days. This is called the 'minor illness' (Phase 1) and in many cases, this may be the only illness (abortive poliomyelitis).



If the infection progresses, the 'minor illness' is followed by the 'major illness' (Phase 2) after 3–4 days. The fever comes on again (biphasic fever), along with headache, stiff neck and other evidences of meningitis. This marks the stage of viral invasion of the CNS. Sometimes the disease does not progress beyond this stage of aseptic meningitis (non-paralytic poliomyelitis). In those proceeding to the paralytic stage, flaccid paralysis develops. Paralysis is focal in distribution initially, but spreads over the next 3–4 days. Depending on the distribution of paralysis, cases are classified as spinal, bulbar, bulbospinal and encephalitic forms



Pathology

Poliovirus selectively damages motor and autonomic nervous system. Chromatolysis of the Nissl substance in cytoplasm occurs. This is followed by changes in the nuclei and pericellular infiltration. The process is reversible until this stage. The functions can be restored within 3–4 weeks. Later neurons undergo necrosis and the process becomes irreversible. The most commonly affected areas are as follows:

- Anterior horn cells of the spinal cord
- Vestibular nuclei
- III–VII nerve nuclei (associated with good prognosis)
- IX–XII nerve nuclei (associated with difficulty in swallowing, pooling of saliva)
- Vital centres in the medulla (centres for respiration and circulation)
- Nuclei in the roof of the cerebellum
- Motor cortex

The following areas are not affected:

- White matter of spinal cord
- Cerebellar hemispheres
- Non-motor part of the cerebral cortex

Predisposing Factors

- Tonsillectomy
- Adenoidectomy
- Tooth extraction
- Physical exercise
- Intramuscular injections

Classification

Poliomyelitis is classified into the following types: (Table 11.54)

TABLE 11.54 Classification and Clinical Features of Poliomyelitis

Classification	Clinical Features
Phase 1 (No CNS involvement)	
Inapparent infection	Asymptomatic
Abortive polio	Low-grade fever which does not exceed 39.5°C, sore throat, nausea, vomiting, headache, unlocalised abdominal pain, constipation, loss of appetite, malaise. Recovery will be complete.
Phase 2 (Frank cases with CNS involvement)	
Non-paralytic poliomyelitis (aseptic meningitis) • Non-specific illness (similar to abortive polio) • Preparalytic poliomyelitis	 Prodrome Intense headache, nausea and vomiting Stiffness of neck, trunk, back and legs (nuchal–spinal signs); recovers within 2–10 days Paralysis of bladder may be present Imminent paralysis but soon reverts back to normal
Paralytic poliomyelitis • Spinal • Bulbar • Bulbospinal • Encephalitic forms	Muscle pain, spasm, return of fever. This is followed by rapid onset of flaccid paralysis which is complete within 72 hours.

I. Inapparent (silent infection)

II. Abortive polio

III. Non-paralytic aseptic meningitis

1. Non-specific illness
2. Preparalytic poliomyelitis

IV. Paralytic poliomyelitis (0.5%–1%)—Types of paralytic poliomyelitis are discussed in Table 11.55.

V. Less common types

1. Meningitic form
2. Acute cerebellar syndrome with cerebellar involvement
3. Polyneurotic form
4. Arthritic form
5. Myelitic form such as transverse myelitis

Clinical Features

- Fever lasts for about 1–3 days. It has two humps, initial rise of temperature during the first phase of illness and the second rise before the paralytic stage. Fever just before the onset of paralysis
- Recent upper respiratory infection
- Fatigue and muscle pain
- Sudden onset, asymmetrical, LMN palsy (flaccid). In polio, extensors are more involved than the flexors. Muscle nutrition is normal. There is asymmetric patchy paralysis
- Deep tendon reflexes are absent/diminished
- No sensory loss
- Bladder symptoms may be present
- Lower cranial nerves (especially IX and X) are commonly affected (Compare VII cranial nerve is commonly affected in Guillain–Barré syndrome)

Clinical features based on the stage of the disease are as follows:

1. Inapparent infection (asymptomatic)—90%–95% of the children infected by poliovirus are asymptomatic
2. Abortive polio—seen in 4%–8% of the children who are infected by poliovirus. It is characterised by fever, headache, sore throat, nausea, vomiting and abdominal pain. Neurological manifestations are absent
3. Non-paralytic poliomyelitis—seen in 1%–2% of infections
   (a) Non-specific illness—features are similar to abortive polio
   (b) Preparalytic polio
   - Back stiffness—there is pain and stiffness in the neck, back and legs
   - Muscle tenderness
   - Head lag and nuchal rigidity
   - Nuchal–spinal signs—these are elicited by active (Box 11.5) and passive tests (Box 11.6) and resemble aseptic menin-

TABLE 11.55 Paralytic Poliomyelitis

Features	Types of Paralytic Poliomyelitis			
	Spinal Form	Bulbar Form	Bulbospinal	Encephalitic
Incidence	79%	1–2%	19%	<1%
Part affected	LMN lesion of anterior horn cells of spinal cord	Cranial nerves with or without involvement of vital centers (respiratory centre, cardiovascular centre, vasomotor centre)	Both cranial nerves and anterior horn cells of spinal cord. Typically, the upper part of cervical spinal cord (C_3–C_5) is affected resulting in paralysis of diaphragm due to phrenic nerve affliction	Cerebrum
Clinical features	Asymmetrical descending paralysis of muscles of legs, arms and trunk (quadriplegia)	Respiratory insufficiency Difficulty in swallowing, speaking or eating	Any of the symptoms of spinal and bulbar forms	Irritability disorientation drowsiness, coarse tremors. Paralysis may be of UMN type

BOX 11.5 Nuchal–spinal signs: active tests

- *Tripod sign:* Stiffness of the back muscle occurs when attempting to flex the spine in the presence of spinal rigidity. The child tries to keep the neck and back extended with the result that he is unable to sit up unless he flexes his knees and places both his hands behind him to support the trunk so that he assumes a tripod position. This is known as the tripod sign.
- *Kiss-the-knee test:* The child is asked to sit with the legs stretched and straight. Now the child is asked to bend forwards and kiss the knee. The child will not be able to kiss the knee, as this will cause pain. In the process the child will flex the knee. The tense appearance of hamstring muscles can be noted. This is seen in children with spinal stiffness due to muscle spasm and is due to involvement of the reticular substance.
- With the child sitting ask the child to touch the chest with the chin. In presence of nuchal rigidity the child will experience pain while flexing the neck.

BOX 11.6 Nuchal–spinal signs: passive tests

The nuchal rigidity usually precedes the spinal rigidity.

- *Nuchal rigidity:* It appears on the first or second day of the preparalytic phase of poliomyelitis. The neck stiffness is due to lesions in the reticular substance. The neck rigidity in poliomyelitis disappears if the child is kept prone with the head extending beyond the edge of the bed. This distinguishes the neck stiffness of preparalytic poliomyelitis from that of meningitis in which the neck stiffness persists in all the positions. It can be tested in a restless and crying child by taking the head beyond the edge of the table when the head drop and neck stiffness persist in the supine position. However, the same disappears when child is put in the prone position.
- *Head drop sign:* It is seen in both non-paralytic and paralytic poliomyelitis. With the patient in supine position the shoulders are raised off the bed by placing the hands under the shoulder. Usually the head also rises along with the shoulders, but in this case the head lag occurs. Children with poliomyelitis are unable to lift the head or bring it in the position of the trunk, and this is known as head lag. If the diagnosis is uncertain even after the above tests, the following tests should be done to elicit the nuchal rigidity.
- *Kernig's sign:* In the presence of nuchal or spinal rigidity in non-paralytic poliomyelitis, Kernig's sign is positive because of the painful spasm of hamstring muscles (normally the leg can be easily straightened).
- *Brudzinski's sign:* Leg sign and head sign may be positive in non-paralytic poliomyelitis.

gitis. Only the head drop sign is present in both paralytic and non-paralytic polio

- Sensory system is normal in poliomyelitis
- The child is fully conscious in spite of signs of meningitis
- During this stage intramuscular injections should be avoided because these may precipitate the paralysis (provocative paralysis). Physical activities can also precipitate the paralysis. So, physical activities should be avoided for 1–2 weeks. The child may be put on bed rest
- Bulging of anterior fontanel may be seen in infants with open fontanels. Lumbar puncture should be avoided
- Reflexes—in early stages of non-paralytic poliomyelitis the reflexes are normal. DTRs may be exaggerated or diminished about 12–24 hours before the onset of paralysis. The superficial reflexes (cremasteric, abdominal, spinal and gluteal) are diminished initially. Deep tendon reflexes are affected about 8–24 hours after the depression of superficial reflexes. Their depression is an indication for impending paralysis. They are absent with the onset of paralysis (Fig. 11.28)

4. Paralytic poliomyelitis—seen in about 0.5%–1% of children infected by poliovirus. In addition to the features of non-paralytic and abortive

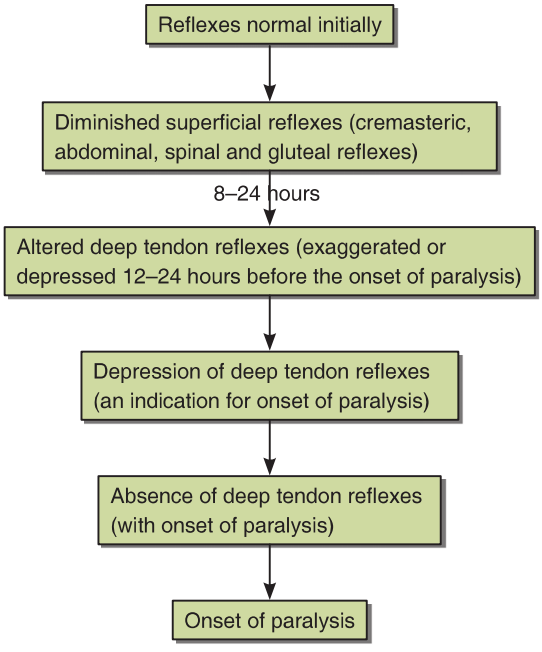


FIGURE 11.28 Reflexes in poliomyelitis.

poliomyelitis, there is weakness of one or more muscle groups. Flaccid paralysis is seen in paralytic poliomyelitis. Localised muscle spasm, muscle pain, tenderness and hypertonia are due to lesions in the brain stem, spinal ganglia and posterior columns. Tightness of muscles may be generalised or localised. It may be due to involvement of the ANS, irritability of the anterior horn cells or functional changes in the muscles themselves. The tightness of the muscles is commonly observed in the tendoachilles, hamstrings and quadriceps. Clinical manifestations depend on the site of involvement

(a) Spinal form—severe headache, fever, severe muscle pain, paraesthesia, hyperaesthesia, tremors and diminished DTRs precede the asymmetrical flaccid paralysis of the spinal muscles. Involvement of the diaphragm and the intercostal muscles cause respiratory difficulty. Autonomic involvement can lead to urinary retention and constipation. The muscles involved in spinal form of poliomyelitis are listed in Table 11.56

(b) Bulbar form—there is weakness of motor part of one or more cranial nerves. This may be associated with or without dysfunction of vital centres of respiration and circulation. The clinical features are as follows:

- Inability to swallow (IX and X nerves)
- Nasal twang (palatal and pharyngeal weakness—IX and X nerves)
- Pooling of saliva and secretions (IX and X nerves)
- Nasal regurgitation of fluids (palatal paralysis—IX and X nerves)
- Hoarseness of voice, aphonia (paralysis of vocal cords—IX and X nerves)
- Rope sign positive—hyoid bone is pulled posteriorly causing an acute angulation between the chin and the larynx due to weakness of hyoid muscles
- Irregular and shallow respiration (involvement of vital centres in the medulla)
- Cardiac arrhythmias, changes in the pulse and blood pressure (damage to the vasomotor centre in the medulla)—there can be a transient rise in the blood pressure, which falls subsequently. Pulse is rapid, weak and thready. The skin becomes dusky red and mottled. Patients become restless and anxious, confused, delirious and comatose

(c) Bulbospinal form is a condition where the features of both the bulbar and spinal forms are seen

TABLE 11.56 Muscles Involved in Spinal Form of Poliomyelitis

Part of the Body	Muscles Involved
Neck	Muscles of neck
Lower limb	Quadriceps, tibialis anterior, peroneal muscles
Upper limbs	Deltoid, biceps, triceps
Thorax	Intercostal muscles, diaphragm
Abdomen	Abdominal muscles, muscles of posterior abdominal wall
Back	Muscles of the back

(d) Polio encephalitis—irritability, disorientation, delirium and drowsiness are seen. Convulsions may be seen. The paralysis may be of UMN type

Complications of Paralytic Poliomyelitis

- Musculoskeletal—residual paralysis, atrophy of muscles involved, bony deformities, contractures, flail limb due to complete paralysis of all the muscles of a limb
- Pulmonary—acute pulmonary oedema, pulmonary embolism due to immobilisation, diaphragmatic paralysis, respiratory failure due to respiratory muscle paralysis
- Cardiac—transient hypertension, hypertensive encephalopathy, cardiac arrhythmias
- Gastrointestinal—gastric dilatation (acute), superficial intestinal erosions (single or multiple)
- Skin—bedsores
- Electrolytes—hypercalcaemia, nephrocalcinosis, hypercalciuria due to immobility
- Infections—UTIs and hypostatic pneumonia are common

Respiratory Paralysis

It is one of the important causes of increased mortality in children with poliomyelitis. Respiratory paralysis is seen in the following conditions:

- Spinal poliomyelitis with paralysis of respiratory muscles such as intercostal muscle and diaphragm
- Bulbar poliomyelitis with paralysis of motor cranial nerve nuclei
- Bulbospinal poliomyelitis with respiratory muscle paralysis and bulbar paralysis

INVESTIGATIONS

These are done if there is AFP to differentiate from other causes.

- Virus isolation—the virus is present in the throat and faeces. The virus cannot be isolated from the throat after first week of onset of paralysis. It can, however, be isolated in the stools from onset to 8 or more weeks after the paralysis. The rate of detection is more during the first 2 weeks after the onset of paralysis. Virus isolation can also be done from CSF, oropharynx and urine in the early stages. It can be cultured from throat, urine and stool.
- Serology—rise in titre of polio antibodies in paired sera. This cannot differentiate between wild and vaccine virus strains.
- CSF examination—CSF shows a moderate increase in cells (polymorphonuclear leucocytes initially and then later lymphocytes) and protein. Sugar and chloride levels are normal. This is useful in differentiating polio from other causes of AFP.

Treatment

Treatment should be started once the diagnosis is suspected. One should not wait for confirmation of diagnosis from the laboratory. The child should be treated in a hospital if there is progression of paralysis, marked drowsiness, bulbar involvement or development of complications such as aspiration pneumonia, cardiac or respiratory dysfunction. The aim of treatment is to minimise residual paralysis and disability, and to promote recovery. It varies with the stage of the disease and severity of paralysis.

1. Abortive polio—patient should be treated with analgesics, sedatives, bed rest. Exertion should be avoided for 2 weeks.
2. Non-paralytic and paralytic polio—there is no specific treatment. Patient should be treated symptomatically for 2–3 weeks. The principles of treatment are as follows:
   (a) Strict bed rest—the risk of trauma and paralysis is more in fatigued muscles, hence is the requirement of bed rest. Frequent changes in posture should be done to avoid bedsores.
   (b) Sedatives—mild sedation can be given but should be avoided in patients with bulbar and encephalitic forms. In both these conditions, these drugs may interfere with the monitoring of the level of consciousness.
   (c) Proper positioning of body—the limbs are placed in neutral position so that muscles

get maximal relaxation. Pillows, rolled towels or sand bags can be used. Plaster of paris cast may be needed for this purpose. A firm bed is desirable. Additionally, following can be done for proper body alignment to prevent skeletal deformity:

- Straight trunk and hip
- Slight flexion of knee to 5°
- Dorsiflexion of ankle to 90° with support to the sole by foot-boards or sand bags
- Prevention of external rotation by placing rolled towels

(d) Pain relief—hot moist packs are applied to the muscles to relieve the pain and spasm (Sister Kenny's treatment). Analgesics are helpful in the relief of pain. Massage and intramuscular injections should be avoided in the acute phase.

(e) Hydration and diet—hydration should be maintain. Diet should be nutritious and balanced. Nasogastric feeds may be given if required.

(f) Bowel and bladder care—laxatives should be given to relieve constipation. Bladder retention should be managed by intermittent catheterisation.

(g) Antibiotics—intramuscular injections should be avoided.

(h) Respiratory support—the examiner should observe for respiratory paralysis. Mechanical ventilation may be required in cases with respiratory failure. Suction of the pharynx should be done in cases with bulbar poliomyelitis. Tracheostomy may be needed in certain cases.

3. Treatment after acute phase is over—it aims at recovery of muscle power, improvement of functional skills, ambulation and prevention of deformities.

(a) Physiotherapy

- Passive movements of the joints should be started as soon as the pain and spasm are relieved. This helps in preventing deformities and joint stiffness. This also helps stimulate proprioceptive impulses from muscles and tendons to improve the muscle power. Training of weak muscles by suitable exercises should be done.
- Active exercises are advised to strengthen the weakened muscles.
- Orthosis may be helpful for ambulation.
- Warm moist fomentations with soft towels to relieve pain.

(b) Surgical management—orthopaedic surgery for fixed deformities and contractures should be done after 2 years.

Rehabilitation

Patients with residual paralysis should be provided with calipers and crutches. The rehabilitation should be given in the hospital and home.

Prognosis

- Prognosis is bad for older children and for patients with sudden onset of illness with high fever.
- Mortality ranges from 5% to 10% and is mainly due to respiratory failure.
- Recovery of the paralysed muscles takes place in the next 4–8 weeks and is usually complete after 6 months, leaving behind varying degrees of residual paralysis. Maximum recovery occurs in the first 6 months and slow recovery may continue up to 2 years.
- Postpolio residual paralysis is said to be present when no more recovery is seen especially after 2 years. However, apparent improvement of the function of the affected limbs can be seen due to the child using the unaffected muscles compensating for the lost function.

Prevention

1. Proper hygiene
2. Immunisation—immunity induced by vaccines is type-specific. There is no cross-reactivity between various strains. Two types of vaccines are available:

(a) Oral polio vaccine (Sabin) contains live attenuated poliovirus. This vaccine induces both humoral and local intestinal cellular

responses. Contraindications to live polio vaccine are as follows:

- Immunodeficiency
- Malignancy
- Children on long-term steroids
- HIV infection/AIDS
- Children allergic to neomycin, streptomycin or polymyxin B

(b) Injectable polio vaccine (Salk) contains killed poliovirus

Eradication of Poliomyelitis

The World Health Assembly committed the member nations of the World Health Organization (WHO) for global eradication of poliomyelitis. Polio eradication is defined as the absence of clinical cases of poliomyelitis for at least 3 years and the absence of detectable wild poliovirus from communities. The goal for eradication of polio is defined as 'no case of clinical poliomyelitis should be associated with wild poliovirus'. The aim is to ensure that wild polioviruses are not present anywhere in the world. The WHO adopted the following four strategies to eradicate polio:

1. Achieve and maintain high routine immunisation of infants under 1 year of age with at least three doses of oral polio vaccine.
2. Administer supplemental doses of oral polio vaccine to all children under 5 years of age under pulse polio immunisation programme.
3. Surveillance for wild poliovirus through reporting and laboratory testing of AFP cases.
4. Mop-up vaccination through intensive house-to-house campaigns in areas where wild polio transmission is identified. This breaks the final chain of virus transmission.

An area is declared as polio-free by the WHO when the following three conditions are satisfied:

1. At least 3 years of zero polio cases due to wild poliovirus.
2. International standard is maintained in the efforts for disease surveillance.
3. Each country should demonstrate the capacity to detect, report and respond to imported polio case.

SURVEILLANCE OF AFP

All cases below 15 years of age with AFP should be reported, so that poliovirus transmission can be detected by early collection of stools in all such cases.

Stool Collection

The stool from a case of AFP should be collected and sent for confirmation of wild poliovirus. The following points should be remembered while collecting the stools:

- Two specimens 24–48 hours apart within 14 days of illness (2 stool specimens with an interval of 2 days within 2 weeks of onset of paralysis).
- Thumb-sized specimen 8–10 g of stool to be collected and stored at a temperature below 8°C.
- Specimen should be collected in a plastic screw cap container.
- Use of laxatives to collect stools should be avoided.
- The specimen should be placed directly into the bottle.
- The rim of the container should not be soiled.
- The bottle should not be filled up to the rim.
- Specimen should be sent to a WHO-accredited laboratory in good condition without desiccation or leakage.
- Cold chain should be maintained while transporting the stool specimen.

Sixty-Day Follow-Up

The 60-day follow-up should be done in the following cases:

- Acute flaccid paralysis cases with inadequate stools specimen collection
- Isolation of wild poliovirus
- Isolation of vaccine type poliovirus

The 60-day follow-up should be done between 60th and 90th day of certain categories of AFP to determine the presence or absence of residual paralysis. It should not be done before 60th day of the onset of paralysis.

Even the presence of mild residual paralysis should be considered as residual paralysis.

TABLE 11.57 Classification of AFP Cases for Surveillance

Classification of AFP cases	Criteria
Confirmed polio case	Wild poliovirus is isolated from stool
Non-polio acute flaccid paralysis	Wild poliovirus is not isolated from adequate stool specimens or No residual weakness after 60 days of observation in a case with inadequate stool examination.
Compatible with polio (a case should be considered as polio case for purpose of surveillance)	Stools specimen examination not done or inadequate stool specimens are collected Residual weakness present 60 days after the onset of paralysis 60-day follow-up not done Absconded before 60 days Died within the observation period of 60 days

Virologic Classification

The children with AFP can be classified as confirmed polio cases or non-polio AFP cases depending on the isolation of wild virus in the stools and 60-day follow-up (Table 11.57). This is useful in polio surveillance. Confirmed polio and cases that are compatible with polio should be reported so that activities to control the spread of polio can be initiated around that area.

FLOPPY INFANT

Floppy infant refers to an infant with severely reduced muscle tone, most often due to an insult in the foetal or neonatal period. There is decreased resistance to passive range of movements. These infants usually have variable degree of muscle weakness.

Look if the infant looks well or sick.

Child appears normal	Child appears sick
SMA type I	Birth asphyxia
Congenital myopathies	Septicemia
Congenital muscular dystrophy	Intraventricular haemorrhage
Down's syndrome	CNS infection
Hypothyroidism	Maternal drugs—sedation with diazepam or magnesium sulphate

AETIOPATHOGENESIS

Central Nervous System Causes

A child may be floppy as a result of pathology in the CNS.

Cerebral Hypotonia

It occurs due to lesion in brain. The causes are summarised in Table 11.58.

Spinal Cord Disorders

- Hypoxic ischaemic myelopathy
- Traumatic myelopathy
- Congenital malformations—spinal dysraphism
- Trauma
- Myelodysplasia

TABLE 11.58 Cerebral Causes of Floppy Infant

Classification	Causes
Cerebral cortex	Cerebral hypoxia Cerebral palsy
Cerebellum	Cerebellar ataxia
Chromosomal disorders	Prader–Willi syndrome Trisomy 21 Lowe's syndrome Acid maltase deficiency and GM1 gangliosidosis Zellweger syndrome
Chronic non-progressive encephalopathy	Atonic cerebral palsy Kernicterus Cerebral malformation Congenital cerebellar ataxia
Peroxisomal disorders	Neonatal adrenoleukodystrophy
Metabolic disorders	Inborn errors in metabolism—aminoaciduria, organic aciduria Mucopolysaccharidosis, cerebral lipidosis
Degenerative	Tay–Sachs disease Metachromatic leukodystrophy
Miscellaneous	Birth trauma Benign congenital hypotonia Intracranial haemorrhage

Peripheral Nervous System Causes

Anterior Horn Cell Disorders

Hereditary

1. Spinal muscular atrophy (SMA)
   - Proximal acute infantile SMA (Werdnig–Hoffman disease)
   - Late infantile SMA
   - Juvenile (Kugelberg–Welander syndrome)
2. Hexosaminidase A deficiency
3. Glycogen storage disorder—type II (Pompe's disease)

Acquired. Poliomyelitis is an important acquired cause of floppy infant. The poliovirus infects the anterior horn cells.

Disorders of Nerve Roots, Plexuses and Peripheral Nerves

- Polyneuropathies—Guillain–Barré syndrome
- Chronic inflammatory demyelinating polyradiculoneuropathy
- Hereditary motor and sensory neuropathy
- Acute motor axonal neuropathy
- Giant axonal neuropathy
- Familial dysautonomia
- Peripheral neuropathy—acute intermittent porphyria, tyrosinemia type I, Chediak–Higashi syndrome, familial amyloid polyneuropathies, paraneoplastic polyneuropathy, toxic neuropathies, drugs (isoniazid, vincristine, zidovudine)

Neuromuscular Junction Disorders

- Myasthenia gravis
- Infantile botulism
- Following intake of drugs that block neuromuscular junction (aminoglycosides, magnesium)

Disorders of Muscles

1. Myopathies
   - Congenital myopathies, mitochondrial myopathy, congenital myotonic dystrophy
   - Metabolic—glycogenosis type II and III, lipid storage myopathy
   - Nutritional—protein energy malnutrition, rickets (acrobatic rickets), scurvy, carnitine deficiency
   - Endocrine myopathies—thyroid (hypothyroidism, cretinism), hyperparathyroidism, hyperaldosteronism (adrenal cortex)
2. Muscular dystrophies
3. Polymyositis/infantile myositis
4. Glycogen storage disease (Pompe's disease)

Skeletal and Connective Tissue Disorders

- Marfan's syndrome
- Ehlers–Danlos syndrome
- Cutis laxa
- Osteogenesis imperfecta
- Arthrogryposis multiplex congenita

Metabolic Causes

- Renal tubular acidosis
- Hypercalcaemia
- Hypokalaemia
- Hypoglycaemia
- Rickets

CLINICAL FEATURES

1. Flailness/hypotonia
   - Abnormal postures—frog-like posture, rag-doll posture on ventral suspension
   - Diminished resistance to passive movements
   - Abnormal joint mobility
2. Delay in motor milestones
3. Floppy child—slips on holding

INVESTIGATIONS

- Chromosomal analysis (Down's syndrome)
- Creatinine phosphokinase (muscular dystrophy)
- Nerve conduction velocity (neuropathies)
- Muscle biopsy (myopathies, muscular dystrophy)
- Tensilon test (myasthenia gravis)
- Urine screening tests (metabolic disorders)
- Thyroid screening (hypothyroidism)

- Serum lactate and CSF lactate
- MRI imaging of brain (cerebral disorders)

COMPLICATIONS

- Respiratory infections
- Orthopaedic problems such as scoliosis, club foot, contractures
- Aspiration of feeds

TREATMENT

- Prevention of complications
- Physiotherapy
- Adequate nutrition
- Genetic counselling for chromosomal disorders and inborn errors in metabolism

SPINAL MUSCULAR ATROPHY

These are degenerative diseases of motor neurons.

SMA Type I a (Werdnig–Hoffman Disease)

It is associated with degeneration of anterior horn cells.

Clinical Features

- H/o sluggish foetal movements
- Marked hypotonia
- Poor sucking
- Dysphagia
- Weak cry
- Pooling of secretions in the pharynx
- Fasciculations of tongue
- Absent deep tendon reflexes
- Lower limbs affected more than the upper limbs
- Proximal muscles affected more than the distal muscles
- Death due to respiratory failure by 2 years of age

Investigations

- EMG—spontaneous fibrillation potentials
- Reduced interference pattern on voluntary contraction
- Muscle biopsy—atrophy of muscle fibres

SMA Type I b

- Onset—between 3 and 6 months of age
- Less fulminant course
- Lifespan more than 10 years

SMA Type II (Dubowitz Disease)

- Onset—between 6 and 18 months of age
- Manifests in the first year of life
- Survival beyond 10 years of life
- The child is not able to walk or stand

SMA Type III (Kugelberg–Welander Syndrome)

- Onset—after 18 months of age
- The child can walk for some period

SMA Type IV

It occurs in adults. The lifespan is normal.

INVOLUNTARY MOVEMENTS

Involuntary movements are abnormal movements which are not subject to control of volition.

TYPES

The involuntary movements are of following types:

1. *Athetosis:* Slow, sinuous, writhing movements more marked in the distal extremities. These occur due to a lesion in putamen. The causes are as follows:
   - Infection—encephalitis
   - Wilson's disease
   - Injury
   - Kernicterus
   - Drug-induced—phenothiazines, L-dopa
   - Cerebral palsy
2. *Ballismus:* Violent flinging movements or rotational excursion of limbs (usually proximal). They affect the neck and trunk also. Ballismus disappears during sleep and is commonly associated with structural lesions in the contralateral subthalamic nucleus. It can be of

various types depending on the part of the body involved:

- Hemiballismus—one half of the body is involved
- Monoballismus—a single limb is involved
- Paraballismus—both the legs are involved

3. *Chorea:* Semi-purposive (or quasi-purposive), non-repetitive, jerky, brief, irregular movements which appear to flow from one part of the body to another. Part of the brain affected is the caudate nucleus. It may occur in isolation or in association with athetosis, as choreoathetosis. It is increased by stress and disappears during sleep.
4. *Dystonia:* Simultaneous contraction of agonist and antagonist groups of muscles results in abnormal postures that are transiently sustained. Part of the brain affected is putamen.
5. *Epilepsy* should be differentiated from other types of involuntary movements.
6. *Fibrillations/fasciculations/myoclonus:* Fibrillations occur due to contraction of individual muscle fibres. Fasciculations occur due to contraction of a motor unit of muscles. Myoclonus is described as brief, sudden, involuntary, repetitive, instantaneous jerk-like contractions of a muscle or group of muscles.
7. *Tremors:* Rhythmical, distal oscillatory movements of a part of the body around a fixed point. They occur due to rapid alternating contractions and relaxations of the agonist and antagonist muscles. They can be fine or coarse, regular or irregular and can occur at rest or during activity.
8. *Tetany:* It is due to hypocalcaemia.
9. *Tardive dyskinesia:* It is due to writhing movements of tongue and face that occur due to intake of certain drugs.
10. *Tics:* Spasmodic, repetitive stereotyped movements which are exaggerated by stress. These may affect any muscle group.

The type of involuntary movement varies according to the site of lesion in the brain (Table 11.59).

Chorea

These are brief, rapid, jerky, non-repetitive, quasi-purposive involuntary movements chiefly involving the face, tongue and the limbs. The movements dart from one muscle group to another. They are increased by stress and excitement and disappear during sleep. The proximal parts are more involved than the distal parts.

Aetiology

The causes of chorea are as follows:

1. Sydenham's chorea—rheumatic autoimmune vasculitis
2. Infections
   - Encephalitis—postencephalitic chorea
   - Toxoplasmosis
   - Coxsackie virus
   - Echovirus
   - Varicella encephalitis
   - Haemophilus influenza B meningitis
   - Neurosyphilis

TABLE 11.59 Types of Abnormal Movements

Types of Abnormal Movements	Level of Lesion/Pathophysiology
Athetosis	Lesion in putamen
Ballismus	Lesion in contralateral subthalamic nucleus
Chorea	Lesion in caudate nucleus. Acetylcholine and GABA are decreased and dopamine is increased or normal
Dystonia	Lesion in putamen
Epilepsy	Lesion in cerebral cortex
Fasciculation	Chronic degeneration of the anterior horn cells
Fibrillations	Denervation hypersensitivity of single muscle fibre
Myoclonus	Infection, head or spinal cord injury, stroke, brain tumours, kidney or liver failure, lipid storage disease, chemical or drug poisoning
Tremors	Neurological disorders such as multiple sclerosis, neurodegenerative disorders such as parkinsonism, traumatic brain injury, drugs such as amphetamines, caffeine Mercury poisoning
Tetany	Increased excitability of the nerves due to hypocalcaemia
Tardive dyskinesia	Drug-induced such as neuroleptics

- Rubeola
- AIDS encephalopathy
- Infectious mononucleosis

3. Endocrine—thyrotoxicosis
4. Drugs
   - Anticonvulsants—phenytoin and carbamazepine
   - Lithium
   - L-dopa
   - Phenothiazines
   - Oral contraceptives
   - Toxin
   - Alcohol
5. Haematological
   - Polycythaemia rubra
   - Sickle cell anaemia
6. Metabolic causes
   - Hepatic encephalopathy
   - Uraemic encephalopathy
   - Hypernatraemia
   - Hypocalcaemia
   - Wilson's disease
7. Familial—chorea acanthocytosis
8. Connective tissue disorder—systemic lupus erythematosus

Types

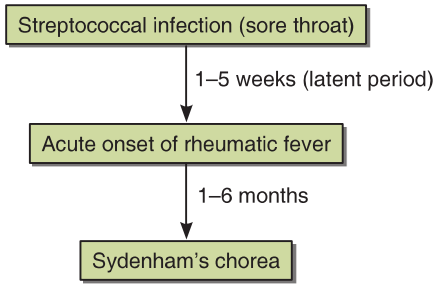
- Rheumatic chorea—seen in children who had an attack of rheumatic fever
- Chorea paralytica—tone is decreased. In 2% of cases, the child is bedridden due to hypotonia
- Hemichorea—affect one side of the body; involves entire half of the body sparing the face
- Paralytic chorea—in severe cases there is muscle weakness; affected side is hypotonic
- Chorea gravidarum in pregnancy
- Maniac chorea—chorea associated with excessive excitement
- Chorea mollis—hemiplegia due to severe hypotonia and weakness
- Huntington's chorea—autosomal dominant inheritance seen in adults and characterised by dementia
- Senile chorea—seen in old age

Rheumatic Chorea

It is also known as St. Vitus dance, chorea minor or Sydenham chorea. It is a delayed complication of acute rheumatic fever. The involuntary movements involve the face, tongue and the limbs. Emotional and behavioural abnormalities are seen few days or weeks before the onset of chorea. The child may be restless, aggressive or excessively emotional.

Pathogenesis

- It follows infection by Group A β-haemolytic streptococci and is seen in 20%–30% of patients with rheumatic fever. Molecular mimicry between antigens of Group A β-haemolytic streptococci and central nervous system is the basis for development of this condition.
- Latent period between streptococcal infection and chorea is 6 months



Epidemiology

- Typical age of onset of rheumatic chorea is 8–9 years. It is rare under 5 years of age.
- It is more common in females.
- Predisposing factors are overcrowding and poor hygiene.
- There is genetic predisposition.

Clinical Features

Onset of rheumatic chorea can be acute and sudden, or gradual and insidious progressing over weeks. Features are as follows:

- Associated movements are exaggerated.
- Attention deficit.
- Blessing sign—if the hands are stretched forwards there is dropping and lifting of the hand.
- The proximal parts are more involved than the distal parts. The movements are worsened during

purposeful movements, excitement, fatigue, emotion and stress. The movements occur at rest and disappear during sleep.

- Choreic hand—there is flexion at the wrist and extension at the metacarpal and interphalangeal joints
- Dinner fork sign—dinner fork deformity (spooning sign). The child may be asked to stretch out the hand and spread the fingers and hold them parallel to the floor with the palms facing the floor. The affected arm is hyperextended at the elbow. The forearm is pronated, wrist flexed and the metacarpophalangeal joints are extended. This gives an appearance of a dinner fork. There are abnormal movements at the wrist and the shoulder.
- Emotional lability—the patient shows abnormality in their emotions.
- Facial grimacing—the child may be accused of making faces; frowning, raising eyebrows, pursing the lips, smiling and bizarre movements of the mouth.
- Generalised hypotonia—decreased resistance to passive movements. Joints can be hyperextended. Child can adopt biazarre positions.
- Gait disturbances—clumsy gait.
- Handwriting—deterioration in handwriting may manifest as macrographia. In severe cases, the handwriting is illegible and is not readable.
- Hung up reflex—with the child sitting on the bed with the legs hanging freely, the knee jerk is elicited. The extension at the knee joint is maintained for some time before the leg comes down. This is called hung up reflex and occurs on the affected side.
- Hypometric saccades—the patient undershoots the target frequently. Occasional undershooting can be normal. Extreme hypometric saccades are suggestive of basal ganglia lesions.
- Involuntary movements—involve the extremities and face, occur at rest and disappear during sleep. They involve the distal parts first and then spread to the proximal muscles and face and tongue.
- Jack in box tongue, darting tongue, chameleon tongue, trombone tongue, adder tongue, snake tongue—the tongue moves in and out (involuntary protrusion and retraction) when the child is asked to open his mouth and protrude his tongue.
- Loss of fine motor control—child may be punished for clumsy handling of objects. The child frequently drops things from hands and spills. He is also unable to fasten the buttons.
- Milkmaid sign/milking sign/relapsing sign—inability to maintain a steady grip. The grip is waxing and waning as happens during milking of cow.
- Motor impersistence—the patient is asked to extend the arms and spread their fingers. The fingers cannot be maintained in a steady position due to hypotonia. The fingers moves as if playing a piano. Child cannot keep still.
- Neuropsychiatric symptoms—fidgetiness, behaviour change, personality change, psychological symptoms relapsing and remitting, aggressive behaviour, frequent mood changes, increased irritability, easy distractibility, impulsivity, attention deficit and hyperactivity, transient psychosis, obsessive–compulsive behaviour.
- Pronator sign—hyperpronation of hands due to loss of tone in the antagonistic muscles. The child is not able to hold the arms above the head with both the palms facing each other. Pronation of the affected arm takes place, so that the palm faces anteriorly or outwards.
- Quasipurposive movements—these start with an abnormal movement in which the child tries to show as if it was done with some purpose. For example, when random movement of the hand placed on the table occurs, the child would pretend to search for some object on the table.
- Reflexes—hung-up deep tendon reflexes.
- Speech—speech is slow, slurred, explosive speech, dysarthric audible click may be heard.
- School performance—deterioration.
- Tone decreased—hypotonia, may progress to chorea paralytica.
- Tics may be associated with chorea.
- Weakness of muscles.
- Rheumatic valvular lesions occur in 60%–80% of the children with chorea. Arthritis and joint involvement may be seen in 30% of the cases with chorea.

Differential Diagnosis

- Wilson's disease
- Drug-induced chorea (phenothiazine, phenytoin, carabamazepine, lamotrigene)
- Systemic lupus erythematosus
- Hyperthyroidism

Investigations

- EEG shows irregular slowing of wave patterns.
- MRI shows increase in size of basal ganglia.
- Chest X-ray may show cardiomegaly due to carditis which may be associated with carditis or valve defects.
- ECG shows changes in carditis.
- Echocardiogram shows cardiomegaly or valve defects.

Treatment

It resolves with treatment. Even without treatment, it resolves in 6–8 weeks. The treatment includes the following:

- Rest
- Supportive care
- Drugs—phenobarbitone 3–5 mg/kg, diazepam 0.04–0.1 mg/kg, etc.

If there is no improvement with these measures, the following drugs are used:

- Sodium valproate 10–40 mg/kg for 3–6 months (increases GABA levels), haloperidol (blocks dopa) 0.25–2 mg/kg/day. In two doses tardive dyskinesia may be seen as a side effect.
- Chlorpromazine 1–3 mg/kg.

These should be continued for 2–4 weeks after clinical improvement. Anti-inflammatory drugs should be given if there is evidence of rheumatic activity. Resistant cases can be treated with plasmapharesis or pimozide. Secondary prophylaxis with penicillin should be given to prevent further streptococcal infection. The following combination drugs can be tried if the child does not respond to the above treatment:

- Sodium valproate and haloperidol
- Benzodiazapine and haloperidol
- Phenobarbitone and largactil

Other measures include immune therapy with plasma exchange and intravenous immunoglobulins.

Complications

- Minor neurological impairment
- Behavioural disturbances
- Choreic epilepsy
- Complications due to associated endocarditis

Prognosis

It is a self-limiting condition with spontaneous remission lasting for 1 week to 3 months. It may recur in few cases. Waxing and waning of symptoms can be present up to 10 years. Minor neurological impairment may remain with an abnormal EEG. The risk of recurrence is present in the first 1–2 years in about 20% of the cases.

Fasciculations

Fasciculations are fine, rapid, irregular, involuntary and inconstant visible twitching movement of large groups of muscle fibres or the whole motor unit. It may be a benign condition or associated with motor neuron lesion. It occurs over the wasted muscle. The muscular contraction is of fine amplitude and is not able to move the adjoining joint.

Method of Bedside Demonstration

- They are spontaneous and usually seen as ripples underneath the skin or sometimes as clinically visible contractions.
- They may be evoked by mechanical stimulation. The degenerating muscle (and not a fully degenerated muscle) is suddenly tapped. Usually a big muscle such as biceps, deltoid or calf muscle is chosen. They are absent in a fully degenerated muscle.
- Fasciculation of the tongue—the tongue is kept relaxed in the floor of the mouth for demonstration of fasciculation. It should not be protruded.

Significance

- Fasciculations are seen in the muscles undergoing active degeneration. It signifies chronic degeneration of anterior horn cells or their homologue cranial nerve nuclei.
- In the absence of wasting, fasciculations have no significance. They are then known as benign fasciculations.

Associated Conditions

Fasciculations are seen in the following conditions:

- Benign fasciculations
- Lower motor neuron lesions
- Werdnig–Hoffman disease
- Amyotrophic lateral sclerosis
- Kennedy disease
- Oraganophosphorus poisoning
- Benzodiazepine withdrawal
- Fatigue
- Myasthenia gravis
- Magnesium deficiency

Prognosis. If fasciculation disappears from a muscle, it signifies that the muscle is totally degenerated and the anterior horn cells are completely destroyed. This carries poor prognosis.

Fibrillation

It refers to the rapid, irregular and unsynchronised contraction of single muscle fibres. It is seen when the muscle fibre loses contact with its innervating axon. It is a state of hyperirritability (denervation hypersensitivity) of single muscle fibre and cannot be detected by naked eye examination. It usually signifies complete denervation of the muscle. It does not occur in healthy children and can be diagnosed by EMG. The causes are as follows:

- Lower motor neuron disease
- Severe peripheral nerve disorders
- Myopathies

Differences between fasciculation and fibrillation are given in Table 11.60.

TABLE 11.60 Differences between Fasciculation and Fibrillation

Features	Fasciculation	Fibrillation
Part involved	Involvement of motor units	Involvement of single muscle fibre
Visibility	Can be seen	Cannot be seen
Significance	May be physiological or pathological	Always pathological
EMG	EMG shows large diphasic or multiphasic action potential	EMG shows short duration spike potential

Myoclonus

It refers to quick, lightning-like contractions of a muscle or group of muscles. It usually involves only one hand or a group of muscles in the upper arm or leg or a group of facial muscles, but it may involve many muscles at the same time. Hiccups are present when it involves the diaphragm. Myoclonus may be seen in normal people when they are asleep.

Associated Conditions

Conditions associated with myoclonus are as follows:

- Hepatic failure
- Renal failure
- Cardiac arrest
- Viral encephalopathy
- Metabolic disorders
- Hypoxia
- Head injuries
- High doses of antihistamines
- Antidepressants (amitriptyline) bismuth, levodopa
- Opioids

Triggering Factors

- Light
- Sudden noise
- Sudden movement

Treatment

- Offending drugs should be stopped
- Dialysis for renal failure
- Hepatic failure should be treated
- Blood sugar should be maintained at normal levels
- Sodium valproate can be used

Tremors

These are rhythmic movements that occur due to rapid alternating contraction and relaxation of muscles. These are triggered by stress and strong emotions. The causes are as follows:

- Anxiety—the tremors are fine and rapid.
- Benign essential tremor—mild and non-progressive or slowly progressive tremor that starts on one side of the body and may involve the other

side within a period of 3 years. Hands are mainly involved but it can also involve head, voice, tongue, legs and trunk. It may be associated with mild gait disturbances.

- Cerebellar tremors—these occur in cerebellar lesions and are also known as intention tremors. These increase as the hand approaches an object that has to be picked.
- Endocrine causes—thyrotoxicosis.
- Flapping tremors (asterixis, swing beating tremors)—it refers to an irregular, abrupt, brief loss of posture in outstretched hands. This occurs in hepatic failure, renal failure, respiratory failure and poisoning with certain drugs. This tremor resembles the beating of bird's wings. The patient is asked to stretch the hand forwards with the hands dorsiflexed at the wrist. The wing beating movements at the wrist joint can be seen.
- Hysterical tremor—it is seen in the body involving one side of the body with no characteristic distribution. The tremors get exaggerated when observed.
- Psychogenic tremors can occur during rest or during postural or kinetic movements Intention tremor syndrome is seen in children aged 6 months to 2 years with severe malnutrition. It is thought to be due to magnesium deficiency as it responds to treatment with magnesium and the CSF magnesium is also low.
- Kwashi shakes—it is characterised by tremors, parkinsonism, rigidity, bradykinesia and myoclonus. It is seen from 6 days to several weeks after starting high protein diet in severely malnourished children.
- Orthostatic tremor—it is characterised by >12 Hz rhythmic muscle contraction that occurs in the legs and trunk immediately after standing.
- Parkinson tremor—it is usually seen in elderly. Early onset Parkinson disease can be seen in children. It is classically seen as pill rolling movements of hand. It is increased by stress and emotions.
- Physiological tremors—these occur in normal children and are not significant.
- Rubral tremors—these are slow coarse tremors seen in lesions of red nucleus. They can occur during rest.

Treatment

1. Medical treatment—it depends on the cause.
   - Essential tremor can be treated with β-blockers.
   - Parkinson tremor can be treated with dopaminergic or anticholinergic agents.
   - Cerebellar tremor does not respond to medical treatment.
   - Dystonic tremor can be treated with diazepam, anticholinergic drugs and botulinum toxin.
2. Physiotherapy—coordination and balancing exercises improve muscle coordination and control and reduce tremors.
3. Surgical treatment—helpful if tremors are severe and not controlled by medical treatment.
   - Thalamotomy
   - Deep brain stimulation by placing implantable electrodes to send high frequency electrical signals to the thalamus

Tetany

Tetany is increased neuromuscular irritability due to low ionic calcium in blood.

Clinical Features

- Irritability
- Muscle cramps
- Peripheral paraesthesia
- Triad of carpopedal spasm (adduction of fingers and thumb with partial flexion at metacarpophalangeal joint), laryngismus stridulus and convulsions
- Dysphagia
- Dyspnoea
- Abdominal colic

Signs

Latent tetany can be elicited by the following signs:

- Trousseau's sign—inflating a sphygmomanometer cuff above the systolic pressure precipitates the carpopedal spasm. In carpal spasm, there is flexion of metacarpophalangeal joints with

extension of interphalangeal joints. The flexed thumb takes its position in between the index and the middle fingers (opposition of thumb). This is known as *main d'accoucheur* or obstetrician's hand. Pedal spasm is less frequently demonstrated. Latent tetany is best recognised by eliciting this sign.

- Chvostek's sign—tapping the facial nerve in front of the ear (at its exit from the stylomastoid foramen) leads to brief twitching of the facial muscles.
- Erb's sign—muscular contractions can be produced by application of subthreshold electrical stimulation.
- Peroneal sign—tapping the peroneal nerve at the neck of fibula produces plantar flexion and adduction of the foot (pedal spasm).

Investigations

- Serum calcium level—hypocalcaemia. Normal serum calcium level is 9–11 mg/dL (ionic fraction is 4.5–5.6 mg/dL)
- Serum electrolytes—in presence of alkalosis the ionic fraction is decreased
- ECG—prolonged Q-T interval

Treatment

- Calcium gluconate can be infused.

Tics

Tics are spasmodic involuntary repetitive, non-rhythmic stereotyped movements such as eye blinking, grimacing of face, throat clearing. The patient blinks the eye without any irritation in the eye or clears the throat in the absence of any pathology in the throat. These are often exacerbated by stress and may affect any muscle group. Tics are classified into three groups:

1. Transient tics of childhood
2. Chronic tics
3. Gilles de la Tourette syndrome—life-long condition, which is inherited as autosomal dominant. It has four components; all may not be present in every patient. These symptoms may wax and wane and are always enhanced by stress and anxiety
   - Motor tics—associated with numerous fluctuating movements of the face, eyelids, neck and shoulders
   - Vocal tics—these include throat clearing, sniffing, barking, coprolalia, echolalia (repetition of words addressed to the patient), palilalia (repetition of one's one words) and echo kinesis (limitation of movement of others). Vocalisations are uncontrollable and frequently jeopardise the patient's social interaction with other children
   - Obsessive–compulsive behaviour—this includes touching, licking, repetitive thoughts and motor actions
   - Attention deficit hyperactivity disorder—more than 50% incidence

Treatment

The tics should be treated when they interfere with the child's normal activities. Following measures have shown some benefit in these children:

- Behaviour management
- Biofeedback programmes
- Drug therapy—haloperidol, penfluridol, clonidine

Dystonia

Simultaneous contraction of agonist and antagonist group of muscles results in twisting and repetitive movements or abnormal postures that are transiently sustained.

Causes

1. Primary
   - Hereditary
2. Secondary
   - Birth injury
   - Wilson's disease
   - Trauma
   - Infection
   - Poisoning—lead poisoning
   - Drugs—therapeutic doses of phenytoin or carbamazepine may cause progressive dystonia; neuroleptics cause tardive dystonia

Types

- Generalised

- Focal (cervical, blepharospasm, oculogyric crisis, oromandibular, laryngeal, focal hand dystonia)
- Segmental—affect adjoining parts of the body
- Intermediate
- Acute dystonic reaction

Treatment

1. Medical—the following drugs can be used in the treatment of dystonia:
   - Antihistamine—diphenhydramine is useful in the treatment of oculogyric crisis.
   - Anticholinergics—benzatropine inhibits neurotransmitter acetylcholine.
   - Muscle relaxants—clonazepam can be used. Botulinum toxin injection in the affected muscle may provide some relief for about 3–6 months.
   - Dopamine agonists—can be used for dopamine responsive dystonia.
   - Baclofen.
2. Surgical—extreme cases not responding to medical treatment, surgical denervation of selected muscles can be done.
3. Deep brain stimulation can be used for severe generalised dystonia.

MICROCEPHALY

Microcephaly is defined as a head circumference that measures more than three standard deviations below the mean for age and sex.

CLASSIFICATION

Microcephly can be classified as primary and secondary depending on the cause.

I. Primary/genetic microcephaly

1. Inherited chromosomal anomalies
   (a) Autosomal recessive
   (b) Autosomal dominant
   (c) X-linked
2. Syndromes

II. Secondary/non-genetic microcephaly

Primary Microcephaly

It is also called true microcephaly or microcephaly vera.

Primary or genetic microcephaly is most often caused by genetic abnormalities that interfere with the growth of the cerebral cortex. It is present at birth and is associated with static developmental anomaly of the brain. Cerebral cortex is disproportionately small. The child is mentally retarded.

1. Inherited chromosomal anomalies—it has three patterns of inheritance, namely autosomal recessive, autosomal dominant and X-linked. Differences between autosomal recessive and autosomal dominant primary microcephaly are given in Table 11.61
   (a) Autosomal recessive inheritance
   - Most common type
   - Both parents are unaffected but carry the gene for microcephaly. There is 25% chance of each child getting affected. The affected child inherits abnormal gene from both the parents
   - Microcephaly is present at birth
   - Characterised by non-progressive mental retardation
   - The child has a typical appearance with slanted forehead, prominent nose and ears, severe mental retardation and

TABLE 11.61 Differences between Autosomal Recessive and Autosomal Dominant Microcephaly

Features	Autosomal Recessive Microcephaly	Autosomal Dominant Microcephaly
Inheritance	The affected child inherits abnormal gene from both the parents.	The affected child inherits abnormal gene from one of the parents
Phenotype	Typical appearance with slanted forehead, prominent nose and ears, severe mental retardation	Non-distinctive facies
Seizures	Prominent	Readily controlled
Mental retardation	Severe	Mild to moderate

prominent seizures. Surface convolutional markings of the brain are poorly differentiated. Brain is small in size with small cerebral cortex

(b) Autosomal dominant

- Rare
- One of the parents is affected and has 50% chance of transmitting the abnormal gene
- The child has non-distinctive facies with upslanting palpebral fissures, hypertelorism, forehead slanting (mild), prominent ears, missing teeth, short stature, receding small forehead, weak eye muscles and thumb hypoplasia
- Psychometric testing is normal or shows mild intellectual impairment. Mental retardation is not as severe as that in autosomal recessive microcephaly
- Head size may be four standard deviation below the mean for gestational age
- Normal linear growth
- Neurosonogram shows no obvious structural abnormalities
- MRI shows abnormal development of brain with small cerebellar and cerebral hemispheres and pachygyria

(c) X-linked microcephaly—there is 25% chance of a son getting affected

2. Syndromes
   - Down's (21-trisomy) syndrome
   - Edward's (18-trisomy) syndrome
   - Cri-du-chat (5 p-) syndrome
   - Cornelia de Lange syndrome
   - Rubinstein–Taybi syndrome
   - Smith–Lemli–Opitz syndrome

Diagnosis

1. Primary microcephaly is diagnosed by exclusion of the following conditions:
   - Craniostenosis (Table 11.62)
   - Malformation syndrome
   - Secondary causes
2. Antenatal diagnosis is done by serial ultrasonogram measurements.

TABLE 11.62 Differences between Microcephaly and Craniostenosis

Features	Microcephaly	Craniostenosis
Prominent bony ridge on palpating the suture	Absent	Common
X-ray	Minimal sutural line	No sutural line
CT scan	Sutures	Sutures are fused

3. Identification of gene responsible for microcephaly helps in genetic counselling and prenatal diagnosis.

Secondary Microcephaly (Non-genetic)

Secondary microcephaly is due to an insult to the growing brain. The insult may occur in utero or during period of rapid growth and results in deceleration or arrest of brain growth. The causes are as follows:

- Radiation
- Infections—TORCH infections (congenital), meningitis or encephalitis (acquired)
- Drugs—foetal alcohol, foetal hydantoin
- Malnutrition
- Metabolic causes—hypoglycaemia, phenylketonuria
- Hyperthermia
- Hypoxic-ischaemic encephalopathy
- Endocrine causes—hypothyroidism and hypopituitarism
- Trauma—birth injuries

Differences between primary and secondary microcephaly are given in Chapter 3.

CLINICAL FEATURES

- Mental retardation
- Delayed motor milestones
- Delayed speech
- Hyperactivity
- Seizures
- Difficulty in coordination and balance

INVESTIGATIONS

- Screening for infections—toxoplasmosis, cytomegalovirus, rubella, HIV
- X-ray skull—periventricular calcification in cytomegalovirus infections, diffuse calcification in toxoplasmosis
- CT scan for calcifications
- MRI for structural abnormalities of brain
- Phenylalanine levels in the mother
- Urine screening tests
- Fasting urine and blood aminoacid analysis
- Thyroid screening tests
- Karyotyping

TREATMENT

- The aim of management is to find out the cause and avoid further progression of the condition.
- Specific treatable causes should be treated—thyroxine replacement for hypothyroidism.
- Nutritional supplementation.
- Drugs to control seizures, hyperactivity and other neuromuscular symptoms.
- Genetic counselling is needed for patients with genetic disorders.

PREVENTION

The following steps are helpful in prevention of microcephaly:

- Prevention of child birth after 35 years of age—for preventing Down's syndrome.
- Maternal screening for TORCH infections and providing adequate treatment.
- Thyroid screening in the newborn.
- Adequate nutrition.
- Health education for mother to avoid alcohol and drugs such as hydantoin during antenatal period.
- Genetic counselling.

MACROCEPHALY

This is defined as head circumference more than two standard deviations above the mean or beyond 97th percentile for normal population of same age, sex, race and region (see also chapter 3). The causes are as follows:

- Hydrocephalus
- Hydranencephaly
- Subdural haematoma
- Osteopetrosis
- Megalencephaly
- Intracranial tumours
- Benign increased ICT

MEGALENCEPHALY OR MACRENCEPHALY

It is a condition where the weight and size of brain is more than average for the age and sex of the child. Later, this may present as macrocephaly as the enlarged brain pushes the cranium. It may be associated with early onset childhood seizures, motor deficits, mental retardation and mild cognitive impairment. Megalencephaly may be seen in the following conditions:

- Normal variant with abnormal cerebral cytoarchitecture
- Neurocutaneous syndromes—tuberous sclerosis, neurofibromatosis, Sturge–Weber syndrome
- Cerebral gigantism (Sotos' syndrome)
- Metabolic disorders—leukodystrophy, lipidosis, histiocytosis, mucopolysaccharidosis

INVESTIGATIONS

- Screening for infections—toxoplasmosis (hydrocephalus)
- X-ray skull shows diffuse calcification in toxoplasmosis
- CT scan should be done for calcifications and hydrocephalus
- MRI should be done for structural abnormalities of brain

TREATMENT

It is symptomatic and supportive and depends on the cause. Anticonvulsants should be given for seizures.

PROGNOSIS

It depends on the underlying cause and the associated neurological disorders.

HYDROCEPHALUS

The term is derived from *hydro* (water) and *kephale* (head). Hydrocephalus refers to accumulation of CSF within the ventricles or cavities of brain due to either of these—increased production of CSF, obstruction to its flow or failure of its absorption in arachnoid villi.

CIRCULATION OF CSF

The CSF is secreted from the choroid plexus of lateral ventricles, which is also the main site of CSF production. It is also secreted from the capillary endothelium of brain parenchyma. The choroid plexus is innervated with both adrenergic and cholinergic nerves. Stimulation of adrenergic nerves decreases the CSF production whereas stimulation of cholinergic nerves increases its secretion.

Cerebrospinal fluid secretion depends on the flow gradient that exists between the ventricles and the venous systems. The CSF flows from the lateral ventricles to the third ventricle through foramen of Monro on both sides. From the third ventricle the CSF passes to the fourth ventricle via aqueduct of sylvius. From the fourth ventricle the CSF passes to the Cisterna magna by foramen of Magendie and Luschka. At the foramina of Magendie and Luschka, the CSF exits the brain. In the subarachnoid space the CSF is absorbed by the arachnoid villi, which in turn drain into the channels of sagittal sinus (Fig. 11.29).

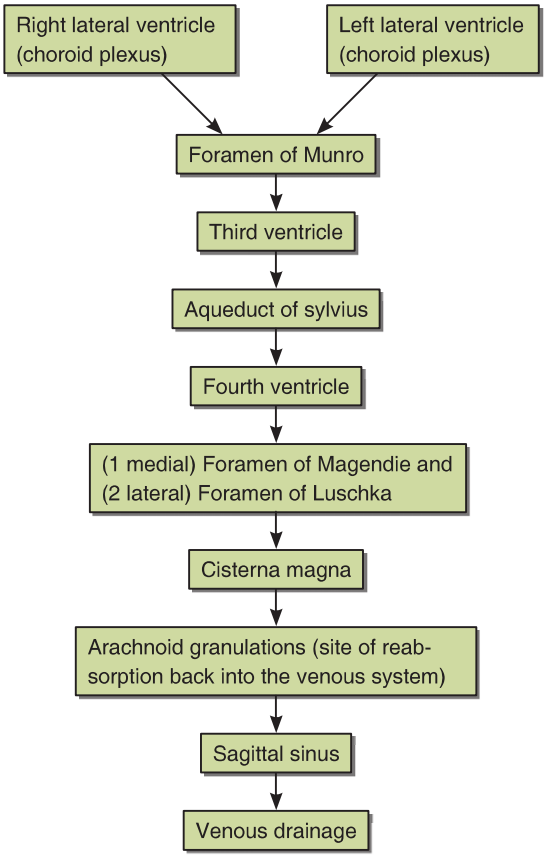


FIGURE 11.29 Circulation of cerebrospinal fluid.

PATHOGENESIS

Normal rate of CSF secretion is about 20 mL/day. Hydrocephalus occurs as a result of any of the following mechanisms, either alone or in combination:

- Increased production of CSF
- Obstruction in flow to the CSF
- Decreased absorption of CSF (Table 11.63)

Response to Increased CSF Pressure

The following changes occur as the CSF pressure increases:

- Absorption of CSF occurs at the ventricles (transventricular absorption) and along nerve root sleeves
- Dilatation begins at the temporal and frontal horns first
- Elevation of corpus callosum
- Thinning of cerebral mantle
- Stretching or perforation of the septum pellucidum
- Enlargement of third ventricle downwards

TABLE 11.63 Pathogenesis of Hydrocephalus

Pathogenesis	Causes
Increased production	Choroid plexus papilloma
Obstruction to the flow of CSF through the ventricular system and subarachnoid space	Obstruction of the interventricular foramina by inflammatory exudates, tumours or blood clot Congenital stenosis/atresia of cerebral aqueduct. Obstruction of the foramina of Monro secondary to tumours, haemorrhage, infections or congenital malformations
Decreased absorption	Obstruction to out flow

AETIOLOGY

The hydrocephalus results from the imbalance between the production and absorption of the CSF.

1. Congenital causes
   (a) Intrauterine infections—these cause inflammatory reaction of the ependymal lining of the ventricles which result in obstruction to the CSF flow
      - Toxoplasmosis
      - Rubella
      - Cytomegalovirus

   (b) Congenital malformations
      - Arnold–Chiari malformations type 1 and type 2—a portion of the cerebellum herniates into foramen magnum and causes obstruction to the CSF flow
      - Agenesis of foramina of Monro
      - Arteriovenous malformation—vein of Galen malformation can expand to a large size and, because of its midline position, obstruct the flow of CSF
      - Brain stem malformation—this includes atresia, stenosis or obstruction of the aqueduct of Sylvius and foramina of Luschka and Magendie (Bickers–Adams syndrome is an X-linked disorder associated with hydrocephalus due to stenosis of aqueduct of sylvius, mental retardation and adduction–flexion deformity of the thumb)
      - Congenital toxoplasmosis
      - Cranial defects—sinus venous pressure is increased in achondroplasia, platybasia, craniostenosis which predisposes to increased intracranial pressure
      - Dandy–Walker syndrome—children with Dandy–Walker cyst have a prominent occiput along with hydrocephalus

2. Acquired causes
   (a) Infections
      - Meningitis (tuberculosis and pyogenic)—this results in aqueductal gliosis which leads to hydrocephalus. In meningitis, the ependymal lining of the aqueduct is interrupted. There is glial response which results in complete obstruction
      - Mumps meningoencephalitis
      - TORCH infections
      - Cysticercosis

   (b) Inflammation—brain abscess
   (c) Posthaemorrhagic hydrocephalus—seen in head injury, subarachnoid haemorrhage, cerebral haemorrhage. Predisposing factors are prematurity and vascular malformations
   (d) Choroid plexus papilloma
   (e) Mass lesions (neoplasms)—posterior fossa tumours (medulloblastoma), astrocytoma, ependymoma, leukaemic infiltrates may seed the subarachnoid space and produce communicating hydrocephalus
   (f) Sagittal sinus thrombosis causes increased venous sinus pressure
   (g) Hypervitaminosis A—idiopathic intracranial hydrocephalus may be due to increase in the CSF secretion or increase in the permeability of blood–brain barrier
   (h) Idiopathic

CLASSIFICATION

Hydrocephalus is classified into communicating and non-communicating types on the basis of underlying mechanism. Hydrocephalus is said to be communicating if the obstruction is outside the ventricular system, which occurs usually in the basal systems. Obstruction within the ventricle is most common in the narrow channels of the third ventricle

and aqueduct and may be caused by tumour or congenital anomaly such as aqueduct stenosis.

Communicating Hydrocephalus

It is also known as *external or non-obstructive hydrocephalus*. It can be congenital or acquired and is due to obstruction outside ventricular system especially at arachnoid villi or basal cisterns. There is no obstruction to the CSF flow from the choroids plexus to the arachnoid villi; obstruction lies outside the ventricular system, usually in the basal cisterns or arachnoid granulations. Resorption of CSF is impaired due to scarring and fibrosis that occurs after infection, inflammation or haemorrhage in the subarachnoid space. The causes are as follows:

- Bacterial/tuberculous meningitis
- Sarcoidosis
- Brain haemorrhage
- Arnold–Chiari malformation
- Congenital absence of arachnoid granulations known as Pacchioni's granulations. Functional impairment of arachnoid granulations located along the superior sagittal sinus where the resorption of CSF to the venous system occurs
- Idiopathic (normal pressure hydrocephalus)

Normal Pressure Hydrocephalus

It is a type of communicating hydrocephalus common in adults. Most of the cases are idiopathic and associated with deficiency of arachnoid granulations. Other causes include subarachnoid haemorrhage, head injury and meningitis.

In this condition, cortical atrophy occurs which causes an increase in the ventricular size and thereby the amount of CSF. The cortical atrophy may be due to intermittent rise in the CSF pressure. Continuous CSF pressure monitoring for 24 hours or longer is needed to diagnosis this intermittent elevation of CSF pressure. There is associated urinary incontinence as the cortical control of the bladder is lost due to pressure over the frontal lobe.

Normal pressure hydrocephalus presents with the following features:

- Gait disturbance—magnetic gait (feet appear stuck to floor due to spasticity) and gait apraxia in later stages
- Impairment of recent memory, slow thinking
- Urinary incontinence
- Personality changes
- Dementia—late finding
- Seizures—rare
- Muscle strength—normal
- No sensory loss
- DTRs—increased
- Babiniski's sign—positive
- Release reflexes at later stages due to frontal lobe lesion (sucking, rooting grasp reflexes which are present in the newborn are inhibited by the cerebral cortex as the child grows. Any condition damaging this cortex results in release of these reflexes)

Non-communicating Hydrocephalus

It is also known as *internal/obstructive hydrocephalus*. It can be congenital or acquired. In this type, there is a block in the circulation within the ventricular system, at various sites like foramen of Monro, outlet of fourth ventricle and aqueduct of Sylvius (Table 11.64). It is seen in the following conditions:

TABLE 11.64 Non-communicating hydrocephalus

Level of Obstruction	Causes	Features
Foramen of Munro	Colloid cyst, tumours, haemorrhage, infections, congenital malformations	Dilatation of one or both lateral ventricles, prominent forehead
Aqueduct of Sylvius	Atresia, ependymitis, haemorrhage, aqueductal stenosis, congenital aqueduct gliosis obstruction (Bickers–Adams syndrome)	Dilatation of both lateral ventricle and third ventricle
Fourth ventricle	Subarachnoid haemorrhage, meningitis, Arnold–Chiari malformation types 1 and 2	Dilatation of both lateral ventricle and third ventricle and aqueduct
Foramina of Magendie and Luschka	Dandy–Walker malformation or congenital defect in opening	Prominent occiput

- Tumours (medulloblastoma, astrocytoma)
- Cysts, abscess and haematoma
- Arnold–Chiari malformation
- Cerebellar abscess
- Cerebellar or brain stem haematoma
- Klippel–Feil syndrome

PATHOLOGY

- The ventricles are dilated; ependyma of the ventricles may be disrupted.
- Cortex is preserved, but can atrophy with prolonged pressure from the hydrocephalus.
- Cortical atrophy itself may lead to increased CSF in the ventricular system.

CLINICAL FEATURES

Symptoms

- Headache and vomiting—more in morning in early stages, becomes better on sitting. This is because the CSF is poorly absorbed in lying down position. The headache becomes continuous as the hydrocephalus progresses. Headache does not occur in normal pressure hydrocephalus
- Urinary incontinence presenting as urgency, frequency in the early stages. In late stages there may be diminished awareness to need to urinate (due to destruction of frontal lobe in advanced disease)
- Blurred vision due to papilloedema
- Drowsiness
- Horizontal diplopia—double vision is due to lateral rectal nerve palsy on one or both sides
- Difficulty in walking—spasticity in the lower limbs

Signs

- Macrocephaly—increase in the head circumference of more than 2 cm per month in the first 6 months should raise suspicion of hydrocephalus and should be investigated.
- Sutural separation can be seen or palpated.
- Fontanels—delayed closure; anterior fontanel is bulging, excessively tense and not pulsatile on crying.
- Sunset sign—it is due to failure of upward gaze of supranuclear origin. Pressure on the tectum through the suprapineal recess results in upward gaze palsy. Upper eyelids are retracted and the eye balls are rolled downwards due to hydrocephalic pressure on the mesencephalic tegmentum and paralysis of upward gaze. The upper bulbar conjunctiva becomes visible due to upward gaze palsy. The eyes are pulled down and the upper limbus of the eye is visible. In normal person usually the upper limbus is not visible and is covered by the upper eyelid.
- Scalp veins are dilated.
- Skin over the scalp is thin and shiny and easily visible.
- Macewen sign (crack-pot resonance)—to elicit this sign the child's head should be lifted up from the bed and supported by placing the examiner's hand under the neck. The head is held by one hand above the cot so that the head does not rest on the bed. In children who can sit, this can be done in the sitting position. The examiner's ear is kept near the temporal region of the patient's skull and percuss with an index finger. A sharp tap with the middle finger is given on the parietal region on each side. When the sign is positive, a peculiar cracked pot sound is heard. It is due to separation of sutures in a child having increased intracranial tension. Though it is most useful when the fontanel is closed, a peculiar sound is heard by tapping the head when tension in the intracranial cavity is markedly increased even with an open fontanel. Macewen sign may be present with hydrocephalus, increased intracranial pressure or suture separation. It is also simulated in many normal infants. This test is not significant before the anterior fontanel closes.
- High-pitched cry.
- Pyramidal signs in the lower limbs—the periventricular region contains the pyramidal tract fibre, which supplies the lower limbs. In hydrocephalus the ventricles are stretched due to increased pressure that causes stretching of the above fibres. Hence, plantar extensor reflex and exaggerated DTRs in the lower limbs along with increased tone in the lower limbs are seen.
- Lateral gaze palsy—lateral rectus palsy may be

seen due to the stretching of the trochlear nerve (false localising sign).
- Transillumination—torchlight equipped with a rubber cuff is placed on the skull.. This is done in a dark room. Translucency extending beyond 2–2.5 cm in the frontal area or over 2 cm in the occipital area is abnormal.
- Papilloedema.
- Bradycardia, due to pressure on the brain stem.
- Systemic hypertension.
- Altered respiration and sometimes even apnoea.

Associated Features

- Neurofibromatosis may be associated with aqueductal stenosis which predisposes to hydrocephalus.
- Cataract, cardiovascular defects and deafness may be associated with rubella infections.
- Spina bifida, meningocele and myelomeningocele in the foetus and newborn infants is associated with hydrocephalus.

Variations in Presentation

Clinical features vary depending on the following factors:

1. Age of the patient—clinical features in infants are different from older children and adults as the ventricles can enlarge to a great extent prior to the closure of fontanel
   (a) Newborns
      - Head circumference increases rapidly to more than 97th percentile
      - Bulging anterior and posterior fontanelles (even in upright position)
      - Fretfulness
      - Poor feeding
      - Frequent vomiting
      - Associated features—spina bifida with or without meningocele or meningomyelocele

   (b) Infants
      - Large head size
      - Poor feeding
      - Irritability
      - Decreased activity or sleepiness
      - Vomiting
      - Lack of interest in surroundings
      - Papilloedema is absent bur reduction in vision may be seen
      - Sunset sign

   (c) Toddlers and older children
      - Headache and vomiting—headache is not seen in normal pressure hydrocephalus
      - Neck pain (due to cerebellar tonsillar herniation through the foramen magnum)
      - Horizontal diplopia—double vision (due to unilateral or bilateral sixth nerve palsy)
      - Letharginess and drowsiness
      - Delayed milestones
      - Urinary incontinence
      - Personality changes and memory loss
      - Papilloedema and optic atrophy at later stages
      - Progressive macrocephaly (even when the sutures are closed the pressure results in enlargement of head)
      - Gait disturbances
2. Aetiological factors
   (a) Normal pressure hydrocephalus
      - Impaired bladder control
      - Dementia and progressive mental impairment
      - General slowing of activities
      - Magnetic gait

   (b) Tumours
      - Headache more significant in morning
      - Vomiting

   (c) Arnold–Chiari malformation
      - Shortened occiput
      - Neck pain due to tonsillar herniation
      - Meningomyelocele may be present in the lumbar region

   (d) Dandy–Walker syndrome—prominent occiput
3. Site of obstruction of CSF flow
   (a) At foramen of Munro—frontal prominence

(b) Fourth ventricle—prominent occiput

4. Onset and duration of hydrocephalus
   (a) Acute hydrocephalus (develops over days)
   - Headache in the morning
   - Vomiting in the morning
   - Papilloedema

   (b) Chronic hydrocephalus
   - Headache (intermittent)
   - Behaviour change
   - Decrease in scholastic performance
   - Mental retardation
   - Loss of consciousness
   - Vision problems
   - Hearing problems
   - Seizures
   - Drowsiness
   - Enlarged skull

DIFFERENTIAL DIAGNOSIS

- Subdural effusion—usually follows meningitis
- Chronic subdural haematoma
- Megalencephaly—familial
- Hydranencephaly—cerebral hemispheres are absent or represented by membranous sacs
- Pseudohydrocephalus is a condition in which the size of the head is normal with dwarfed face and body. This is known as Russell dwarf

INVESTIGATIONS

1. Finding the aetiology
   (a) TORCH screening
   (b) CSF analysis—protein level is elevated in postmeningitic and posthaemorrhagic causes of hydrocephalus. Lumbar puncture is done to find out the opening pressure of CSF and also for continuous CSF pressure monitoring. It helps to predict if the normal pressure hydrocephalus is shunt responsive or not, if the opening pressure is more than 100 mm of H_2O it is shunt responsive. If it is less than 100 mm of H_2O it is shunt responsive
   (c) Ventriculography
   (d) Pneumoencephalography
   (e) MRI to find out the level of lesions
2. Confirmation of diagnosis
   (a) X-ray skull
   - Enlargement of skull
   - Widening of sutures
   - Erosion of the clinoid process
   - Thinning out of the skull bones
   - Copper beaten appearance
   - Deepening of the sella turcica
   - Calcification in toxoplasmosis and cytomegalovirus infections

   (b) Ultrasonogram in infants—subependymal and intraventricular haemorrhage
   (c) CT scan—size of the ventricles increased (Box 11.7)
   (d) MRI is preferred for posterior fossa and spinal cord lesions. It may show Arnold–Chiari malformation, periaqueductal or cerebellar tumours (Box 11.7).
   (e) Angiography
   - In cortical atrophy, angiography shows separation of thalamostriate vein from the midline and increased number of curves in the anterior and middle cerebral arteries.
   - In hydrostatic hydrocephalus, there

BOX 11.7 CT scan or MRI criteria for acute hydrocephalus

- Size of temporal horns—more than 2 mm and clearly visible
- Evan's ratio in hydrocephalus—the ratio of largest width of the frontal horns to maximal biparietal diameter will be more than 30% diameter
- Transependymal exudates will be seen as hypoattenuation in the periventricular region in CT scan and hyperintensity in MRI
- Micky mouse ventricles (ballooning of frontal horns and third ventricles). Third ventricle may be herniated into sella turcica
- Sagittal MRI will show upward bowing of corpus callosum due to atrophy of corpus callosum
- Erosion of sella turcica
- Macrocrania

is a separation of thalamostriate vein from the midline in the anteroposterior venous phase
- In advanced cases of hydrocephalus the distance between the insula and the vault of the skull is less than one-third the distance from the vault to the midline due to cortical atrophy

(f) Electroencephalogram should be done if there are seizures

TREATMENT

Medical Treatment

It provides temporary relief and includes the use of drugs which act either by decreasing CSF secretion by choroid plexus (acetazolamide and loop diuretics) or by increasing CSF reabsorption (isosorbide).

- Acetazolamide—inhibits the enzyme carbonic anhydrase (non-competitive reversible inhibition) and thereby decreases the CSF production. Dose is 50 mg/kg/day. If the hydrocephalus gets arrested, no treatment is needed.
- Loop diuretics—furosemide increase water excretion by interfering with chloride binding cotransport system. This causes inhibition of reabsorption of sodium and chloride in the ascending loop of Henle and distal renal tubule. It also inhibits cation-chloride pump that affects water transport into astroglial cells.
- Combination of acetazolamide and furosemide is helpful.

Surgical Treatment

Shunt Procedures

These are done to divert the CSF into the peritoneum, pleura or the right atrium. These involve placement of a catheter which bypasses the obstruction and drains the CSF distal to the obstruction. The excess CSF is drained into the body cavities.

1. Ventriculoperitoneal shunt—most commonly used. Cerebrospinal fluid from lateral ventricle is drained into the peritoneum. The advantage is that the shunt need not be lengthened as the child grows.
   - Upathyaya shunt
   - Pudentz shunt
   - Spitz–Holter shunt
   - Chopra shunt
2. Ventriculoatrial shunt (vascular shunt)—it connects cerebral ventricles to the right atrium of heart through the jugular vein and superior vena cava. This procedure can be done when ventriculoperitoneal shunt is contraindicated as in obesity, peritonitis or after abdominal surgery. The disadvantage is that the shunt has to be lengthened as the child grows.
3. Lumboperitoneal shunt—CSF from the lumbar space is redirected to peritoneal space. It can be done for communicating hydrocephalus, CSF fistula and pseudotumour cerebri.
4. Ventriculocaval shunt.
5. Shunt between lateral ventricle and cisterna magna (Torkildsen shunt)—done in acquired obstructive hydrocephalus.
6. Ventriculopleural shunt—can be used if all other shunts are contraindicated.

Other Surgical Procedures

- Choriod plexectomy
- Choroid plexus coagulation
- Cerebral aqueductoplasty—done for stenosis of a short segment of sylvian aqueduct
- Endoscopic fenestration of floor of third ventricle is done in non-communicating hydrocephalus
- Repeated lumbar puncture—helpful in postmeningitic and posthaemorrhagic hydrocephalus. These usually resolve spontaneously but require prevention of complications until resolution
- Ventricular tapping in infants or open ventricular drainage in older children can be done for rapid onset hydrocephalus to prevent damage to cerebral cortex

Treatment of Associated Conditions

- Treatment of tuberculous/pyogenic meningitis
- Surgery to correct the primary cause—endoscopic third ventriculostomy through an endoscope inserted through the lateral ventricle
- Surgical removal of tumour or other obstruction

Treatment During the Intrauterine Period

Shunting can be done by endoscopic surgery in the antenatal period.

FOLLOW-UP

- Head circumference should be monitored.
- The patients should be taught about the signs of shunt infection or blocks.
- Antibiotic prophylaxis should be advised in patients with vascular shunts before dental procedures or instrumentation.
- Periodic re-evaluation should be done.
- Patients or care givers should be taught about signs of acute or chronic progressive hydrocephalus.

PROGNOSIS

- The prognosis depends on the primary cause of hydrocephalus.
- Children with arrested hydrocephalus may decompensate following minor head injuries or infection.
- Patents with large interventricular haemorrhage develop permanent hydrocephalus and require shunting procedures.
- In hydrocephalus due to tumour, the prognosis depends on the type, location of the tumour and the extent of surgical resection of tumour.
- In normal pressure hydrocephalus, if the gait disturbance precedes mental deterioration, the child responds to shunt but children with mental deterioration and normal gait rarely respond to shunts.
- Initial opening pressure of more than 100 mm of H_2O has good response in children with normal pressure hydrocephalus.
- Children with large ventricles with flattened or invaginated sulci, which indicates entrapment of sulci improves with shunting.

PREVENTION

- Early diagnosis and treatment of CNS infections
- Neural tube defects should be prevented by providing folic acid to the mother
- Mother should be screened for intrauterine infections before conception and treated
- Genetic counselling for genetic disorders

POSTMENINGITIC AND POSTENCEPHALITIC SEQUELAE

Sequelae is defined as residual disability which persists after the termination of acute or subacute illness in a previously normal child. Clinically, there should be no signs of acute infection (fever, meningeal signs). This is supported by normal cell count on CSF examination. There is no exact duration for sequelae to appear. It is arbitrarily designated as 2–4 weeks. Sequelae depend on the causative agents, duration and severity of illness. For instance, severe sequelae appear after encephalitis due to herpes simplex virus infection (causes focal infarcts in brain), deafness is common after *Haemophilus influenzae* infections. The following sequelae may appear in a child with meningitis or encephalitis:

- Intellectual impairment
- Motor weakness
- Visual and hearing defects
- Psychiatric manifestations
- Epilepsy
- Extrapyramidal involvement

The differentiating features between postmeningitic and postencephalitic sequelae are given in Table 11.65.

INVESTIGATIONS

- Cerebrospinal fluid analysis is normal.
- CT scan is indicated if there is any change in symptoms or deterioration in the clinical condition. CT scan is done to look for hydrocephalus, subdural effusion, infarcts, ring lesions and basal exudates.

TREATMENT

Treatment should aim at general care and well-being

TABLE 11.65 Differences between Postmeningitic Sequelae and Postencephalitic Sequelae

Features	Postmeningitic Sequelae	Postencephalitic Sequelae
Age	Pyogenic meningitis—any age TBM—rare at less than 6 months age	Any age
Onset	Acute—bacterial Subacute—TBM	Acute
Progression	Gradual	Rapid
Predisposing factors	CSOM Head trauma Measles (immunodeficiency predisposes to TBM)	Diarrhoea
Seasonal variation	–	+
Epidemic	–	+
Protein energy malnutrition	Common in children with TBM	–
Progression	Gradual—TBM	Rapid
Involvement	Focal neurological signs	Widely distributed signs except in herpes encephalitis
Pathology	Increased intracranial tension	Cerebral oedema
Optic atrophy	More common	Less common
Multiple cranial nerve palsy	More common	Less common
Hydrocephalus	More common	Rare
Meningeal signs	More common	Less common
Mental retardation	Less common	More common
Behavioural problems	Less common	More common
Sleep disturbances	Less common	Common
Involuntary movements	Less common	More common
Decerebrate/decorticate rigidity	Less common	More common
Part of brain affected	Meninges Cranial nerves Cerebral cortex	Cerebellum Extrapyramidal system Hypothalamus
Sequelae	Hydrocephalus Cranial nerve palsies	Minimal brain dysfunction Attention deficit disorder Short attention span

CSOM—chronic suppurative otitis media; TBM—tuberculous meningitis.

of the child and specific treatment of any underlying illness.

1. General care
   - Prevent aspiration
   - Proper feeding technique
   - Nutritional care
   - Anticonvulsants for seizures
   - Splint
   - Bladder care
   - Prevent bedsores
   - Physiotherapy
   - Occupational therapy
2. Specific treatment—antituberculous drugs for tuberculosis
3. Surgical correction—ventriculoperitoneal shunt for hydrocephalus

PROGNOSIS

It depends on the following factors:

- Age—better prognosis in older children.
- Causative organisms—sequelae after infection with herpes simplex virus carry a poor prognosis.
- Severity of meningitis—the more severe the infection, the more severe the sequelae.

DISORDERS OF URINARY BLADDER

Urinary bladder is associated with storage and micturition of urine. This occurs due to complex integration of signals from the bladder.

ANATOMICAL CONSIDERATIONS

It is important to know the muscles of the bladder and the nerve supply to understand the normal and pathological conditions of the urinary bladder.

Bladder Innervation

The bladder is controlled by the following nerve fibres:

1. Parasympathetic fibres from S_2, S_3, S_4 segments—

pelvic splanchnic nerves via nervi erigentes control detrusor contraction resulting in emptying of bladder. During bladder filling, there is inhibition of parasympathetic fibres.

2. Sympathetic fibres—facilitate filling of the urinary bladder. They cause direct relaxation and expansion of the detrusor muscle and keep the urinary tract in constantly active state during bladder filling. They close the bladder neck by constricting the internal urethral sphincter. Sympathetic innervation of the sphincter causes active contraction of the bladder neck during ejaculation. This is important for sexual function in opening the internal sphincter without associated contraction of the detrusor muscle.
3. Somatic fibres—pudendal nerve supplies the external sphincter. This is under voluntary control. However, if the bladder fills to its capacity the voluntary control will be lost and there will be sudden relaxation of external sphincter (Table 11.66 and Fig. 11.30).

Remember: parasympathetic stimulation—passes urine; sympathetic stimulation—stores urine.

TABLE 11.66 Nerve Supply of Bladder

Bladder Innervation	Nerve Supply	Functions
Parasympathetic fibres from S_2, S_3, S_4 segments	Nervi erigentes	Emptying of bladder by contraction of detrusor and relaxation of external sphincter
Sympathetic fibres from sympathetic plexus L_1, L_2, L_3, L_4	Hypogastric nerve	Filling of bladder by direct relaxation and expansion of the detrusor muscle and inhibiting parasympathetic system
Somatic fibres S_2, S_3, S_4 segments	Pudendal nerve	Voluntary control of urination by contraction of external sphincter

BLADDER CONTROL

The newborn and the infants do not have control over their bladder. This control develops as the child grows and is influenced by various factors such as training by the parents, mental development, anatomical defects, psychological problems. The bladder control for day usually develops by one and a half to two years and that for night by 3 years with good training. Bladder is regulated by central and peripheral nervous system. Control of bladder is given in Table 11.67. The following parts are responsible for bladder control:

1. Frontal lobe of brain—the cortical micturition control centre sends *inhibitory* signals to the detrusor muscles to prevent emptying of bladder. This occurs when there is no socially

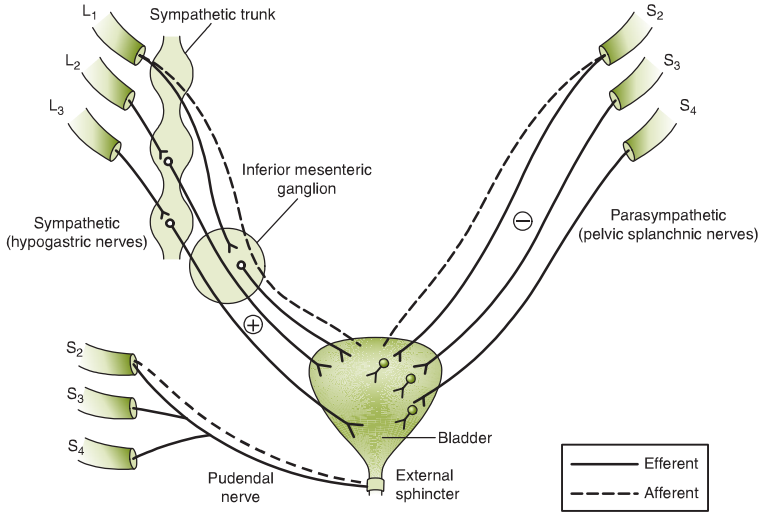


FIGURE 11.30 Nerve supply of bladder.

TABLE 11.67 Control of Bladder

Part	Function
Corticospinal tract	Voluntary control
Urethral reflex loop	From urethral afferent to pudendal nerve. Holds urine in the bladder by constricting the urethra
Detrusor reflex loop	Sphincter relaxation and detrusor contraction
Cerebral loop	Inhibition and switching before filling and voiding
Cord loop	Coordinates urethral sphincter

acceptable place to urinate. Lesion results in loss of voluntary control of the normal micturition reflex.

2. Brain stem—it is the main relay centre between the brain and spinal cord. The pontine micturition centre sends *facilitatory* signals for urethral sphincter relaxation and detrusor contraction and helps in urination.
3. Spinal cord—sacral reflex centre is the primitive micturition centre.
4. Peripheral nerves—these are component of autonomic and somatic nervous system. Normal voiding is a spinal reflex.
5. Muscles of bladder—the following muscles are involved in micturition process:
   - Detrusor muscle
   - Trigone
   - External sphincter muscle (voluntary control)
   - Internal sphincter (autonomic control)
   - Muscles of pelvic diaphragm

NEUROGENIC BLADDER/ NEUROPATHIC BLADDER

It is a condition where the bladder function is affected due to neurological dysfunction. This is due to damage to the nerves that control the bladder functions.

Causes

1. CNS
   (a) Cerebral causes
      - Brain tumours
      - Dementia

   (b) Spinal cord disease
      - Trauma
      - Cord compression
      - Neural tube defects—spina bifida, meningomyelocele, amyotrophic lateral sclerosis, etc.
      - Herniation of intervertebral disc
2. Peripheral nerve injury
   - Peripheral nerve diseases
   - Neuropathies
   - Herniated discs
   - Surgical injury

Pathogenesis

Three types of defect are seen in neurogenic bladder:

1. Interruption of facilitatory and inhibitory pathways descending from brain (UMN)
2. Interruption of afferent and efferent fibres (LMN)
3. Incoordination

Types

Bladder dysfunction can be of spastic or flaccid types depending on the level of lesion (UMN and LMN). Mixed patterns (both flaccid and spastic) can be seen in syphilis, diabetes mellitus, brain and spinal cord tumours, stroke, ruptured intervertebral disk, demyelinating and degenerative disorders, etc. Neurological dysfunction can result in following specific types of neurogenic bladder (Table 11.68):

- Cortical/spastic bladder
- Reflex neurogenic bladder (automatic bladder)
- Autonomous bladder (hypotonic bladder)
- Sensory bladder (atonic bladder)
- Motor bladder
- Detrusor sphincter dyssynergia

Complications

- Bladder diverticula
- Calculus—urinary stone formation
- Excoriation of skin
- Kidney failure
- Infections—urinary tract infections

TABLE 11.68 Types of Neurogenic Bladder

Types of Neurogenic Bladder	Pathophysiology	Causes	Features
Cortical bladder/uninhibited bladder/spastic bladder	Damage to corticoregulatory fibres above the pons	Demyelination Frontal lobe tumours/parasagittal tumours (meningioma) Anterior communicating artery involvement (cerebrovascular accidents) Parkinsonism (in adults)	Detrusor hyperreflexia (frequency, urgency, urge incontinence, sudden uncontrolled evacuation) No residual urine Loss of social inhibition
Reflex neurogenic bladder/automatic bladder/spinal bladder/UMN bladder/contractile bladder	Complete interruption of sensory and motor pathway between sacral spinal cord and brain stem	Traumatic spinal cord Transverse myelitis Loss of bladder sensation	Reflex emptying without warning or sensation (sudden emptying) Incomplete evacuation Inability to initiate micturition Low volume contracted bladder Bilateral pyramidal signs
LMN bladder, autonomous bladder (hypotonic bladder) Detrusor areflexia Areflexic bladder, non-reflex bladder Denervated bladder Acontractile bladder	Lesion in the sacral portion of spinal cord which interrupts the reflex arc controlling the bladder Denervation of muscles innervated from S_2 to S_4 Damage to the sacral center with both afferent and efferent limbs of the arc affected	Cauda equina lesions Conus medullaris lesions Injury to sacral roots and pelvic nerve	Inability to initiate urination normally loss of normal bladder sensation and reflex activity Atonic large bladder Weak or totally paralysed bladder Inability to initiate micturition No reflex activity No bladder sensation Dribbling incontinence Significant residual urine Bladder is emptied by manual pressure
Sensory/atonic bladder	Selective destruction of sensory fibres between bladder and spinal cord or afferent tract to brain. Sensory arc is affected	Peripheral neuropathy Diabetes Tabes dorsalis Cauda equina lesions.	Sensation of bladder filling is absent so that the bladder overflows Large volume, over distension Dribbling incontinence Evacuation with straining Evacuation is incomplete Voluntary micturition intact Hypotonia with residual urine Bulbocavernous reflex, superficial anal reflex absent
Motor bladder Deefferented bladder	Destruction of parasympathetic motor innervation of bladder	Poliomyelitis Peripheral neuropathy Cauda equina lesions Trauma	Painful retention and distension of bladder Inability to initiate micturition In chronic cases there will be over distension with residual urine Bulbocavernous reflex, superficial anal reflex absent
Detrusor sphincter dyssynergia	Incoordination between detrusor and sphincter	Lesion at suprasacral spinal cord Overactive bladder due to UMN lesion	Voiding obstructed resulting in urinary retention Increased residual urine Bladder capacity decreased Bulbocavernous reflex, superficial anal reflex preserved

- Vesicoureteral reflux resulting in hydroureter and hydronephrosis due to reflux nephropathy

Assessment

- Watch the child voiding urine. If there is coordinated detrusor contraction, child can pass urine in a stream. In older children the urine output can be measured as mL/unit time by electronic measuring devices as a measure of detrusor contraction and bladder neck obstruction.
- Crede manoeuvre—manual pressure over the lower abdomen results in emptying of certain types of neurogenic bladder. This method of expressing urine is contraindicated in outlet obstruction and in presence of vesicoureteric reflux.
- Valsalva manoeuvre results in urinary incontinence if the sphincters are weak.

Investigations

- Ultrasound examination to assess the residual urine volume
- Full bladder stress test—fill the bladder to its capacity by urinary catheterisation. Look for incontinence by various procedures like bending, coughing, walking and sneezing
- Urine examination for UTIs
- Voiding cysturtehrogarm/retrograde urethrography to rule out stricture and diverticulae
- Cystoscopy
- Sphincter electromyelography
- Urodynamic studies—based on urodynamic studies the neurogenic bladder can be grouped as given in Table 11.69
- Renal function tests
- Intarvenous urography
- Radionucleotide imaging

Treatment

The aim of treatment is to restore the anatomy and recovery of physiological functions. The child should be able to empty the bladder completely and periodically and control incontinence. The renal functions should be preserved.

Medical Treatment

This includes the use of following drugs:

1. Drugs to enhance the bladder capacity by decreasing the detrusor muscle tone
   - Muscle relaxants—direct smooth muscle relaxant (flavoxate)
   - Anticholinergic drugs—propantheline, imipramine, oxybutynin, hyoscyamine decrease the detrusor contraction and are given for overactive bladder
2. Drugs to enhance the bladder contraction
   - For underactive bladder—bethanechol a muscarinic agonist, stimulates the bladder contractions in patients who retain urine
   - For areflexic bladder and poor detrusor contractions—carbachol, bethanechol, distigmine bromide increases the detrusor contraction
3. Drugs to treat altered urinary sphincter tone (Table 11.69)
   - Beta-adrenergic agonists such as ephedrine increase the tone in the bladder neck
   - Antispasmodics
   - Dyssynergic sphincter—alphalytic, alphamimetic, skeletal muscle relaxants, imipramine
   - Diazepam, baclofen, botulinium toxin type A can be used to relax the sphincters involved in urination

Supportive Care

- Intermittent catheterisation—repeated catheterisation should be done to prevent the bladder from filling completely or an indwelling catheter may be kept in place all the time
- Kegal exercise—to strengthen the pelvic floor muscles

Surgical Treatment

- Widen the sphincter to maximise emptying of the bladder
- Tightening of the sphincter or pelvic floor muscles for better voiding
- Artificial mechanically controlled sphincter impalantation or bladder neck reconstruction for weak sphincter or bladder neck

TABLE 11.69 Classification of Detrusor—Sphincter Dysfunction

Group	Problem	Urodynamic study	Treatment
I	Storage problem	Hyperreflexic detrusor with hyperreflexive sphincter, low capacity	Anticholinergic drugs, smooth muscle relaxants
II	Storage problem	Incompetent sphincter	Alphamimetic
III	Emptying problem	Areflexic or hyporeflexive detrusor and flaccid pelvic floor	Cholinergic drugs Passive voiding by abdominal straining or by Crede manoeuvre or intermittent catheterisation
IV	Emptying problem	Sphincter spasm	Alphalytic, skeletal muscle relaxants, imipramine

- Electrical stimulation of sacral nerve
- Sling surgery
- Surgical diversion of urine externally or into the gut for areflexic bladder
- Ileal conduit or ureterostomy
- Rhizotomy converts spastic bladder into flaccid bladder
- Augmentation cystoplasty for persistent hypertonicity or hyperreflexia or small capacity bladder
- Sphincterotomy for dyssynergic hyperactive sphincter

Preventive Therapy

The following treatment is helpful to prevent complications:

- Antibiotics for treatment of infections and prevent UTIs
- High fluid intake to decrease the risk of UTIs and urinary tract calculi
- Frequent change in position
- Early ambulation
- Decreased intake of calcium to prevent calculus formation

CHAPTER 12

Disorders of Genitourinary System

HISTORY TAKING

A detailed history should be taken to find out the following:

- Anatomy—site and nature of the lesion
- Physiology—which is altered due to the lesion
- Biochemical changes—which could have caused the symptoms (acidosis)
- Microbiology—the causative organism
- Pathology—the nature of the lesion (infection in the renal tract)

History of various parameters, as relevant in a suspected case of genitourinary involvement, is taken.

Age

- Congenital nephrotic syndrome is seen in the newborn.
- Nephrotic syndrome is common between the age of 2 and 6 years.
- Acute nephritic syndrome is common in older children (4–10 years).

Gender

Urinary tract infections are common in females.

Presenting Complaints

The usual presenting complaints are as follows:

- Decreased urine output
- Fever
- Puffiness of face

History of Present Illness

The details of each of the presenting complaints should be taken in chronological order. Some common symptoms related to genitourinary system are as follows:

1. Oedema (periorbital or generalised oedema)
2. Decreased urine output—enquire about the amount of urine passed in the last 24 hours. Table 12.1 shows the interpretation of varying amounts of urine output in a child
3. Frequency of urination—increases in urinary tract infection (UTI). Table 12.2 depicts the normal variation in frequency according to age
4. Haematuria
5. Abdominal pain—ask about the nature, frequency, site, severity, timing, aggravating and relieving factors. The site and nature of pain may give a clue about the clinical condition (Table 12.3)
6. Dysuria—burning micturition or crying during micturition is seen in small children with UTI
7. Pneumaturia—air bubbles may be seen in the urine if there is a fistula between the intestinal tract and the urinary tract
8. Polyuria and polydipsia—occur due to impaired urinary concentration and is seen in obstructive

TABLE 12.1 Urine Output and Its Significance

Urine Output (mL/kg/h)	Significance
>2	Normal
1–2	Acceptable
<1.0	Oliguria
<0.5	Anuria
>4.0	Polyuria

TABLE 12.2 Normal Numbers of Voids per 24 Hour

Age	Normal Numbers of Voids/24 Hour
3–6 months	20
6–12 months	16
1–2 years	12
2–3 years	10
3–4 years	9
12 years—adulthood	4–6

TABLE 12.3 Urinary Conditions Associated with Abdominal Pain

Type of Pain	Clinical Condition
Flank pain/loin pain	Ureteric colic/renal colic.
Dragging pain	Hydronephrosis Polycystic kidney
Suprapubic pain	Urinary tract infection, cystitis and bladder calculus
Colicky pain at renal angle	Renal calculus

uropathy, renal tubular acidosis, diabetes mellitus and diabetes insipidus

9. Nocturnal enuresis—refers to passing urine in the bed during night time
10. Poor urinary stream or dribbling—common in obstructive lesions of urethra. If present since birth, it may be suggestive of posterior urethral valve
11. Colour of the urine
    - Milky—chyluria
    - Smoky urine—in acute glomerulonephritis (AGN)
12. Foul-smelling urine—a feature of urinary tract infections
13. Distension of the abdomen—uniform distension is seen in ascites. Only the lower abdomen is distended due to retention of urine
14. Swellings in the abdomen

TABLE 12.4 General Symptoms and Their Association with Renal Diseases

General Symptoms	Renal Conditions
Fever Malaise Weakness Fatigue Nausea Vomiting Anorexia	Renal failure UTI Renal tubular acidosis Obstructive uropathy

    - Renal mass (polycystic kidney, Wilm's tumour, hypernephroma and hydronephrosis)
    - Urinary bladder distension
15. Extra renal symptoms
    - Non-specific complaints (Table 12.4)
    - Hearing or visual problems (Lowe's syndrome)
16. History of drug intake
    - Nephrotoxic drugs—non-steroidal anti-inflammatory drugs (NSAIDs), penicillamine, anticonvulsants, antimalignant drugs, diuretics and aminoglycosides
    - Rifampicin can stain the urine

History to Rule Out Other Differential Diagnosis for Generalised Oedema

- Dyspnoea, chest pain, orthopnoea, paroxysmal nocturnal dyspnoea and palpitations (congestive cardiac failure [CCF])
- Jaundice, haematemesis, melaena, flapping tremors and altered sensorium (hepatic failure)
- Loss of appetite, loss of weight, skin changes and irritability (features of kwashiorkor—nutritional oedema)
- History of prolonged steroid intake—Cushing's syndrome

History Related to Complications

- H/o headache, vomiting, convulsions, altered sensorium, blindness, facial weakness and hemiplegia (hypertensive encephalopathy and cortical vein thrombosis in nephrotic syndrome)
- H/o dyspnoea, tachypnoea, palpitations and cough (CCF)

- H/o irritability, oliguria and failure to thrive (renal failure)
- H/o bony deformities (renal osteodystrophy)
- H/o waddling gait (renal rickets)
- H/o pain abdomen (peritonitis and renal vein thrombosis)
- Anaemia (not responding to iron)
- Rickets (not responding to standard doses of vitamin D)
- Neurological symptoms such as delay in development and convulsions (Alport syndrome, etc.)

Symptoms in Newborn

- Failure to gain weight or loss of weight
- Irritability
- Poor feeding
- Vomiting
- Abdominal distension

History of Past Illness

- H/o similar illness before (in nephrotic syndrome, there may be a history of recurrence)
- H/o sore throat due to streptococci (predisposes to nephritic syndrome)
- H/o skin infection such as impetigo or scabies (predisposes to AGN)
- H/o jaundice—hepatitis B infection predisposes to nephrotic syndrome
- H/o fever with rash—measles, mumps or chicken pox
- History suggestive of infectious mononucleosis (sore throat, fever, fatigue, weight loss, petechiae, lymphadenopathy and loss of appetite)
- History suggestive of previous UTI
- History suggestive of infective endocarditis (predisposes to nephrotic syndrome)
- H/o gum bleeding and bone pain (malignancy—leukaemia/lymphoma predisposes to nephrotic syndrome)
- H/o fever, dysphagia and arthralgia may be suggestive of collagen vascular disease, which predisposes to nephrotic syndrome

Antenatal History

- Oligohydramnios (in renal problems in the newborn)
- Placental weight increased (more than 25% of the baby's birth weight in congenital nephrotic syndrome—Finnish type)

Neonatal History

- Umbilical cord catheterisation can cause renal artery thrombosis
- History of delay in voiding urine
- History of oliguria

Growth and Development History

Growth retardation is seen in patients with chronic renal failure (CRF) and renal tubular disorders.

Nutritional History

Nutritional history includes feeding problems, loss of appetite and craving for salt.

History of Allergy and Contact

History of contact with a known case of tuberculosis should be noted.

Family History

History of similar illness in the family members is seen in the following conditions:

- Hereditary nephritis
- Congenital nephrotic syndrome
- Infantile polycystic kidney
- Cystinosis (nephropathic cystinosis is an inherited, autosomal-recessive, lysosomal storage disorder caused by defective transport of the amino acid cystine out of lysosomes)
- Nephrogenic diabetes insipidus

CLINICAL EXAMINATION

General Physical Examination

1. Level of consciousness—irritable or altered sensorium in renal failure
2. Appearance—sick-looking child (AGN), well-looking child (nephrotic syndrome) and generalised hemihypertrophy (nephroblastoma and medullary sponge kidney)

3. Face—puffiness of face and dysmorphism (Potter facies)
4. Eyes—buphthalmos, cataracts, intellectual disabilities, aminoaciduria (Lowe's syndrome or oculocerebrorenal syndrome), aniridia (nephroblastoma), retinopathy (hypertensive nephropathy) and retinitis pigmentosa (Laurence–Moon–Biedel syndrome)
5. Oral cavity—tonsillitis may be associated with acute nephritic syndrome
6. Nutritional status—growth retardation in CRF and nephrotic syndrome of long duration
7. Short stature—rickets and Turner's syndrome (Table 12.5)
8. Oedema—pitting (localised or generalised)
9. Pallor—anaemia (in CRF) is usually normocytic normochromic
10. Skin—pyoderma, evidence for bee sting, cafe-au-lait spots (neurofibromatosis associated with renal artery stenosis), maculopapular rash (vasculitis), purpura and Henoch–Schonlein purpura (HSP), butterfly rash and malar rash (systemic lupus erythematosus [SLE]), angiokeratoma (Fabry's disease), Shagreen patch (tuberous sclerosis), ash leaf macule (tuberous sclerosis) and tuft of hair (spina bifida: neurogenic bladder)
11. Nails—dystrophic nails (nail patella syndrome—nephropathy) (Table 12.5)
12. Spine—sacral agenesis (neuropathic bladder) and meningomyelocele (bladder dysfunction)
13. Lymph nodes—generalised lymphadenopathy is seen in patients with leukaemia, lymphoma, SLE and infectious mononucleosis

Vital Signs

- Pulse—significant findings in pulse with their associated conditions leading to renal impairment are given in Table 12.6
- Blood pressure—increased in renal parenchymal involvement
- Temperature
- Respiratory rate

Anthropometry

- Weight
- Height/length—decreased in CRF
- Head circumference—microcephaly in CRF
- Midarm circumference

TABLE 12.5 Various Syndromes Associated with Renal Problems

Syndrome	Renal Problems	Other Features
Turner's syndrome	Renal tract anomalies Horse shoe kidney Duplex ureters Ectopic kidney, abnormal renal vasculature and double collecting system	Short stature Cubitus valgus Broad shield-like chest
Prune belly syndrome	Urinary tract anomalies Urinary tract infections Renal dysplasia Vesicoureteral reflux Megalourethra Urethral stenosis or atresia	Bladder musculature poorly developed Difficulty in evacuating the bladder completely Urethra narrowed
Nail patella syndrome	Nephritis resembling chronic glomerulonephritis	Dysplasia of nails

TABLE 12.6 Significant Findings in Pulse with Their Associated Condition

Clinical Findings	Conditions
Radiofemoral delay	Coarctation of aorta
Absence of pulses	Takayasu's disease

Systemic Examination

Genitourinary System

- Phimosis, ulcer, swelling and vulval oedema
- Scrotal oedema (nephrotic syndrome)
- Bilateral cryptorchidism

Cardiovascular System

- Look for features of congestive cardiac failure. Cardiac failure may be seen in patients with acute nephritic syndrome.
- Anasarca may also be seen in CCF.
- Pericardial effusion may be present in association with anasarca.
- Pericardial rub is seen in uraemia.

Respiratory System

- The patient feels air hunger in metabolic acidosis
- Type of respiration may be thoracoabdominal in presence of ascites

- Anasarca may be associated with hydrothorax
- Basal crepitations may be present in the presence of CCF
- Tonsils may be enlarged with tender cervical lymphadenopathy due to acute streptococcal tonsillitis

Gastrointestinal System

- Abdominal distension (ascites)
- Abdominal mass—Wilm's tumour, hydronephrosis and renal vein thrombosis. Hepatosplenomegaly is seen in SLE, juvenile rheumatoid arthritis, subacute bacterial endocarditis, shunt nephritis and polycystic kidney
- Absence of anterior abdominal wall muscle—prune belly syndrome
- Shifting dullness and distended urinary bladder
- Bruit may be heard over the renal arteries due to thrombosis or stenosis
- Per rectal examination for pelvic mass

Central Nervous System

- Hemiplegia, blindness and convulsions due to thromboembolism may be seen in nephrotic syndrome.
- Hypertensive encephalopathy is a complication of AGN.
- Flapping tremor and delirium may be seen in uraemia.
- In CRF, peripheral neuropathy may be seen.

Skeletal System

- Arthropathy in SLE, juvenile rheumatoid arthritis and HSP
- Features in rickets—short stature, bowing of legs, genu valgus and costochondral beading

INVESTIGATIONS

Urine Examination

1. Reducing substances: Benedict's test is positive in diabetes mellitus and renal glycosuria.
2. Macroscopic examination: Urine is cola coloured in AGN.
3. Microscopic examination: RBC casts and haematuria. Red cell casts indicate glomerular inflammation. Urine for deposits of cells is positive in patients with urinary tract infections.
4. Urine tests for proteins: Standard tests for proteinuria are as follows:
   - Heat coagulation test: Take 10 mL of urine in a test tube and boil the upper part of the tube. If turbidity appears, add six drops of 5% acetic acid. If turbidity is due to the presence of phosphates, it will disappear. If it persists, it indicates that proteins are present. The presence of protein is graded as 1+ to 4+ (Table 12.7).
   - Sulphosalicylic acid test: Add 5–10 drops of 20% sulphosalicylic acid to 5 mL of urine and examine for turbidity. Presence of turbidity indicates proteinuria and is graded according to the increasing amounts of turbidity as 1+ to 4+ (Table 12.8).

TABLE 12.7 Interpretation of Heat Coagulation Test

Observation Findings	Proteinuria	Urinary Protein (mg/dL)
Slight turbidity through which fine letters can be read	1+	15–30
More turbid	2+	30–150
Cloudiness with fine precipitate through which the letters cannot be read	3+	150–300
More cloudy, nothing will be visible	4+	>300

TABLE 12.8 Interpretation and Grading of Sulphosalicylic Acid Test

Amount of Turbidity	Rough Estimation of Proteins
No turbidity	Negative
Slight turbidity just perceptible against a black background	Trace (20 mg/dL)
Turbidity is distinct but without granule formation	1+ (50 mg/dL)
Turbidity is distinct and granular	2+ (200 mg/dL)
Dense turbidity with distinct clumping	3+ (500 mg/dL)
Dense turbidity with solidified large clumps (precipitated protein)	4+ (1000 mg/dL or more)

- Dipstick or Albustick test: It is a method for qualitative assessment of proteinuria. It tells result directly by comparing with colour code given on bottle. Development of green colour indicates presence of protein. The colour ranges from yellow for negative through yellow-green, green to blue-green for positive reactions. Proteinuria is graded from trace to 4+ on the basis of dipstick test.

5. Urine quantification
   - Twenty-four-hour urine quantification—24-hour urine collection is useful for the estimation of glomerular filtration rate (GFR), and quantification of its constituents is useful in nephrotic syndrome.
   - Random (spot) urine quantification—It is useful for screening and follow-up of children with renal disorders; random urine quantification is ideal in nephrotic syndrome.
   - Urinary protein-to-creatinine ratio in a spot sample of urine has been used to estimate proteinuria semiquantitatively, and its significance is summarised in Table 12.9.
6. Urine culture and sensitivity: Collection of urine is best done by percutaneous suprapubic bladder puncture. Significant bacteriuria refers to colony count of more than 100,000 organisms per millilitre and is seen in urinary tract infections.

Blood Examination

- Blood urea and creatinine
- Serum cholesterol
- Serum proteins—total proteins and albumin/globulin ratio

TABLE 12.9 Summarising Spot Protein/Creatinine Ratio and Its Significance

Spot Protein/Creatinine Ratio	Significance
<0.5 (in children <2 years) <0.2 (in children >2 years)	Normal
Between 0.5 and 3.0 (in children <2 years) Between 0.2 and 3.0 (in children >2 years)	Significant but non-nephrotic proteinuria
More than 3.0	Nephrotic proteinuria

- Antistreptococcal antibody titres—ASO titre and anti-DNAse B test
- Serum protein electrophoretic pattern (EPP)
- Complement levels (C_3 and total haemolytic complement activity)

Imaging Studies

- Plain X-rays—renal size, shape and presence of radiopaque calculi
- Ultrasonogram—initial assessment of genitourinary system
- Intravenous pyelogram for renal anatomy and function
- Micturiting cystourethrogram—anatomy of the lower urinary tract, vesicoureteric reflux and posterior urethral valves
- Radionuclide imaging—99mTc-labelled radionuclide scans for the detection of renal parenchymal defects associated with UTI. Commonly used compounds are dimercaptosuccinic acid, diethylene triamine pent acetic acid and mercaptotriacylglycine (MAG-3)

Renal Biopsy

Renal biopsy is helpful in pathological diagnosis of chronic glomerulonephritis, IgA nephropathy, Alport syndrome, etc.

TREATMENT

Treatment is both supportive and specific, according to the type of lesion.

ACUTE GLOMERULONEPHRITIS

AGN consists of a sudden onset of oedema, haematuria (macroscopic or microscopic), hypertension, oliguria, varying degrees of proteinuria and azotaemia. It may follow infection with a variety of bacteria, viruses and parasites. It may also occur as a part of systemic disease or a primary glomerular disease.

HISTORY TAKING

Age

AGN is common in the age group of 4–10 years.

Presenting Complaints

- Puffiness of face
- Decreased urine output
- Red/cola coloured urine

History of Present Illness

The details of each presenting complaint should be asked in chronological order. In addition, the history of associated problems should be checked. History of the following symptoms is usually positive in AGN:

- Haematuria
- Headache (due to hypertension)

History of Past Illness

- Sore throat (streptococcal)—most common cause
- Scabies (complicated by pyoderma)
- Fever due to infections such as hepatitis B, mumps, measles, chickenpox, infectious mononucleosis, malaria, pneumococcal pneumonia and infective endocarditis. Fever may also be due to collagen vascular diseases (SLE, vasculitis, HSP, etc.)
- Drug hypersensitivity
- Diabetes and hypertension
- Prolonged steroid therapy or urticaria (angioneurotic oedema) as a differential diagnosis of moon face
- Guillain–Barre syndrome

Rest of the history is taken as in a case of genitourinary system.

PHYSICAL FINDINGS

General Examination

General examination is characterised by the following features:

- Oedema
- Hypertension
- Haematuria
- Enlarged tonsils with tender cervical lymphadenopathy due to acute streptococcal tonsillitis

Systemic Examination

Cardiovascular System

- Systemic hypertension
- Apex may shift down and out (due to left ventricular dilation and systemic hypertension) and may be forceful in nature
- Loud A_2 (due to systemic hypertension)
- Mitral systolic murmur (functional murmur due to left ventricular dilation) may be present
- Gallop rhythm may be present (left ventricular failure [LVF])
- Rarely, pericardial rub in acute renal failure

Respiratory System

- Bilateral basal crepitations—due to LVF
- Absence of hydrothorax—to differentiate it from nephrotic syndrome

Nervous System

- Features of hypertensive encephalopathy
- Fundoscopy—usually normal

Skin

Children with acute nephritis may have scabies with pyoderma.

CLASSIFICATION

I. Post-infective glomerulonephritis (PIGN)

1. Acute post-streptococcal glomerulonephritis (PSGN)—Causative agents of acute PSGN are as follows:
   - Group A β-haemolytic *Streptococcus*—nephritogenic strains (most common)
   - Group C β-haemolytic streptococci
2. Non-streptococcal PIGN—Causes are as follows:
   (a) Bacterial
   - Infective endocarditis (PIGN may occur as a part of bacterial endocarditis and shunt infection)
   - Septicaemia
   - Staphylococcal infection

- Pneumococcal infection
- Toxoplasmosis
- *Klebsiella pneumoniae*
- Salmonella infection

(b) Spirochetes

- Leptospirosis

(c) Viral

- Varicella
- Measles
- Mumps
- Infectious mononucleosis
- Hepatitis B
- Cytomegalovirus
- HIV
- Herpes simplex

(d) Parasites

- Malaria—*P. malaria* and *P. falciparum*
- Toxoplasmosis

(e) Fungal

- *Candida albicans*

Non-streptococcal PIGN is milder than the PSGN. Treatment of the primary infection produces resolution of the glomerulonephritis.

II. Non-infective glomerulonephritis

1. Primary glomerular diseases:
   (a) Anti-glomerular basement membrane disease
   (b) Idiopathic crescentic glomerulonephritis
   (c) Idiopathic membranoproliferative
   (d) IgA nephropathy
   (e) Alport syndrome (familial nephropathy)
   (f) Membranous nephropathy
2. Secondary glomerulonephritis. It occurs as a part of multisystem disorders:
   (a) Systemic lupus erythematosus
   (b) Polyarteritis nodosa
   (c) HSP
   (d) Goodpasture's syndrome
   (e) Wegener's granulomatosis
   (f) Miscellaneous causes—Guillain–Barre syndrome, irradiation and chemotherapy of renal tumours, serum sickness

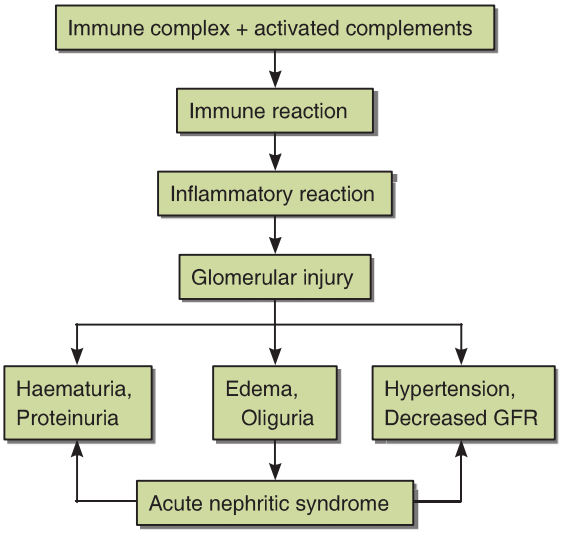
Acute PSGN

It is the most common cause of glomerulonephritis in children. It is mostly caused by group A beta-haemolytic streptococcus. Types of Group A β-haemolytic streptococci involved in AGN are 1, 2, 4, 12, 18, 25, 49, 55, 57 and 60. Of these types, 12, 4 and 49 are commonly involved. Types 4 and 12 cause pharyngitis. Type 49 is mainly responsible for the skin infection (pyoderma). Remember that streptococcal pharyngitis may produce AGN or acute rheumatic fever while streptococcal skin infection produces AGN only

- Age group—2–12 years, commonly after 3 years age. Mainly involves the children from school-going age group
- Gender—males are commonly affected
- Incubation period—Interval between the infection and the development of nephritis will be 1–3 weeks; approximately 10 days from throat strain, and 15 days from skin strain

Pathogenesis

- The complements are activated by the antigen–antibody complexes and cause inflammatory reaction.
- Immune complex + activated complement—this combination leads to immune reaction, which causes glomerular injury. This results in haematuria, oedema, hypertension and oliguria.



- Mechanism of oedema formation—retention of salt and water and hypoproteinaemia.
- Mechanism of hypertension—stimulation of renin–angiotensin–aldosterone axis and hypervolaemia due to salt and water retention.

Pathology

Electron microscopy shows lumpy deposits on the subepithelial side of the capillary basement membrane. Subepithelial electron dense deposits are called humps when they are large.

Immune fluorescent studies show granular deposition of IgG and complement (C_3) along the capillary walls.

Clinical Features

The disease onset is rapid. The clinical features are as follows:

- Puffiness of face
- Cola-coloured urine
- Oliguria (the degree of oliguria corresponds with the severity of the disease)
- Haematuria
- Oedema
- Hypertension
- Proteinuria (<3 g/day)

Incidence of symptoms in children with AGN is given in Table 12.10.

Clinical Course

Acute PSGN resolves spontaneously.

- Complete recovery in 93%–97% cases
- With the occurrence of diuresis, loss of oedema and fall in blood pressure start. This begins within 2 weeks. Hypertension may rarely persist for several weeks
- Gross haematuria disappears by 3 weeks
- Microscopic haematuria may persist for even up to 1 year
- Proteinuria may persist for up to 6 months

TABLE 12.10 Incidence of Symptoms in AGN

Features	Percentage
Haematuria	100
Oedema	90
Proteinuria	80
Hypertension	60
Oliguria	50

Differential Diagnosis

- HSP
- Mesangioproliferative glomerulonephritis
- Polyarteritis nodosa
- Goodpasture's syndrome
- Rapidly progressive glomerulonephritis

Non-PSGN

It is a term which is loosely used to denote all causes of AGN except PSGN. It includes non-streptococcal PIGN and non-infective glomerulonephritis.

Clinical Features

- No latency period between the infection and the onset of symptoms
- Systemic features—petechiae, arthralgia, arthritis and skin rash
- Normal C_3 at presentation or persistently low C_3
- Nephrotic range of proteinuria
- Nephrotic syndrome with nephritic onset
- Family history

INVESTIGATIONS

1. Blood counts with ESR
   (a) RBC count—decreased due to haemodilution
   (b) Total count—leucocytosis (due to glomerular inflammation and not necessarily UTI)
   (c) Differential count—neutrophilia
   (d) Hb%—decreased
   (e) Erythrocyte sedimentation rate—increased
2. Urinary examination
   (a) Macroscopic examination—cola coloured or smoky urine; decreased 24-hour urine volume; urine test for protein—moderate albuminuria
   (b) Microscopic examination—presence of RBC, RBC cast, WBC, granular cast and epithelial cells (RBC cast is diagnostic of acute nephritis)

(c) Specific gravity—decreased due to increased tubular reabsorption
(d) Urine culture and sensitivity—done to rule out UTI
(e) 24-hour urinary protein (proteinuria is usually moderate, less than 50 mg/kg/day)
(f) Spot protein or creatinine ratio (in the first morning urine specimen)

3. Blood biochemistry
   (a) Serum electrolytes—hyponatraemia and hyperkalaemia
   (b) Normal cholesterol (differentiates from nephrotic syndrome)
4. Evidence of streptococcal infection
   (a) Throat swab culture may rarely show β-haemolytic streptococci
   (b) Skin culture
   (c) Raised ASO titre in acute PSGN (more common with throat infection)
   (d) Hypocomplementaemia C_3 and C_4 (C_3 level in active phase is diminished to less than 80 mg%, which returns to normal, that is 100–200 mg%, on recovery)
   (e) Anti-DNAse B is elevated in cases with streptococcal skin infections
5. X-ray chest
   (a) Prominent vascular markings due to hypervolaemia
   (b) Cardiomegaly may be seen in cases with CCF; features of pulmonary congestion may be seen
6. Renal function tests
   (a) Diminished GFR
   (b) Elevated blood urea and creatinine
7. Fractional excretion of sodium less than 1 (because the tubules avidly reabsorb sodium)
8. Urine to plasma creatinine ratio more than 40
9. Ultrasonogram of abdomen—normal or slightly enlarged kidneys
10. Electrocardiogram may show evidence of hyperkalaemia (tall *t*-waves)
11. Renal biopsy—It is rarely indicated in PSGN except under following circumstances:
    (a) Onset with no evidence of preceding infection (clinically and on investigations) or onset of haematuria and infection at the same time
    (b) Absence of evidence for immune complex disease (no rise in antistreptococcal antigens; normal compliments)
    (c) Atypical early features (no latent period, progressive renal failure and nephrotic range of proteinuria)
    (d) Atypical late features
        - Failure of normalisation of RFT within 4 weeks, persistence of oliguria and azotaemia beyond 2 weeks
        - Decreased level of C_3 >6–8 weeks
        - Proteinuria >8 weeks
        - Gross haematuria or macroscopic haematuria of more than 3 weeks
        - Microscopic haematuria >24 months
        - Hypertension lasting more than 1 month even after diuresis sets in; persistence of hypertension >6 weeks
        - Appearance of persistent nephrotic syndrome
    (e) Systemic involvement—clinical picture suggestive of SLE or hereditary nephritis (familial cases with sensory neural deafness and anterior lenticonus)
    (f) Family history of renal disease

MANAGEMENT

AGN may be complicated by labile hypertension. Such patients might have sudden transient rise in the blood pressure. This predisposes them to cardiac failure and hypertensive encephalopathy. Hence, the patients should be admitted in hospital and monitored by recording the blood pressure frequently.

1. *Bed rest:* Strict bed rest is advised until the features of glomerular inflammation and circulatory congestion subside. This can be assumed by the disappearance of oedema, oliguria, haematuria, hypertension, elevated blood urea and RBC casts in urine.
2. *Diet:* Carbohydrate diet is preferred. Mild protein restriction is done in patients with azotaemia. When oliguria is moderate, 0.5 mg/kg/day of protein should be given.
3. *Correction of fluid* and *electrolyte imbalance*

- Sodium and potassium intake should be restricted till urine output increases and blood urea returns to normal values. No added salt diet is advised in children. Potassium-containing foods such as coconut water and fruits are better avoided.
- The fluid intake should be restricted to the output plus the insensible losses. The insensible water loss is the amount of water lost through sweating and respiration. This is calculated as 25 mL/kg for infants and 20 mL/kg for older children (400 mL/m^2). In the presence of gross oedema, the urine output is not replaced; rather, only the insensible fluid loss is replaced. This is called as negative fluid balance.

4. *Diuretics:* Furosemide 1–2 mg/kg is used in the presence of oedema and hypertension.
5. *Antihypertensives:* These are indicated in severe hypertension. Mild hypertension is controlled by dietary restriction of salt and water. Commonly used antihypertensive agents are nifedipine, amlodipine, atenolol and hydralazine. Diuretics are also used. The diastolic pressure must be maintained below 90 mmHg. The blood supply to the cardiac muscles through the coronary vessels usually occurs in the diastole. Hence, increased diastolic pressure can lead to the compromise of this blood supply. When the diastolic pressure increases more than 90 mmHg, nifedipine (0.25–0.5 mg/kg/dose), hydralazine or diazoxide should be given, as these drugs have quick onset of action. A drug with prolonged action (e.g., α-methyldopa 10–40 mg/kg/day in three divided doses) should be added to keep the blood pressure under control. If there is a hypertensive emergency, IV nitroprusside or labetalol is given.
6. *Antibiotics:* Skin infections and pharyngitis should be treated with penicillin or erythromycin for 7–10 days.
7. *Complications* such as CCF, hypertensive encephalopathy and renal failure should be treated.
8. *Dialysis* may be required. Indications for peritoneal dialysis are as follows:
   - Persistent anaemia
   - Hyperkalaemia
   - Severe acidosis
   - Pulmonary oedema
   - Uraemic encephalopathy—convulsions
   - Rapid deterioration of renal functions

COMPLICATIONS

- Acute renal failure
- Hypertensive encephalopathy
- Acute LVF due to labile hypertension
- Infections—urinary tract, respiratory tract, etc.
- Fluid and electrolytic imbalance—fluid overload; electrolyte abnormalities—hyperkalaemia
- Metabolic abnormalities—hypocalcaemia and hyperphosphataemia
- Nephrotic syndrome and chronic nephritis

Acute Renal Failure

Clinical Features

- Severe oliguria or anuria
- Drowsiness, confusion, delirium and even coma may supervene
- Hypertension
- Acidotic breathing (deep sighing, rapid breathing at a regular rate and with a hissing sound is called Kussmaul's breathing)
- Blood urea, creatinine and potassium levels are invariably high with acidosis

Treatment

Acute renal failure should be treated with dialysis if there is prolonged oligouria, fluid overload and life-threatening electrolyte imbalances.

Hypertensive Encephalopathy

Children with AGN have labile hypertension, that is there are sudden fluctuations in the blood pressure. The heart is not able to adapt to these sudden fluctuations as opposed to slow and persistent hypertension. This results in hypertensive encephalopathy.

Clinical Features

- Features of increased intracranial tension—headache, vomiting, convulsion or coma
- Hypertension

- Confusion and delirium
- Though rare, focal neurological signs such as temporary blindness, aphasia, hemiparesis or extensor plantar response may be present
- Papilloedema with retinal exudates and haemorrhages may be present

Treatment

- Antihypertensive drugs such as nifedipine and hydralazine along with supportive management.

Acute LVF

Clinical Features

- Dyspnoea, orthopnoea and PND
- Cough
- Central cyanosis
- Hypertension
- Gallop rhythm, crepitations at lung bases and pulsus alternans

Treatment

- Control the hypertension. Intravenous furosemide is helpful.

MONITORING

- Blood pressure—ideally 4 hourly BP should be taken
- Intake/output chart
- Weight—daily recording of weight helps in suspecting fluid retention
- Renal function—blood urea and creatinine levels should be monitored

FOLLOW-UP

- Monthly urine albumin check-up
- Annual measurement of blood pressure and serum creatinine

PROGNOSIS

The prognosis in children is better than adults. Most cases are self-limited. Oedema and hypertension resolve in a week. Haematuria and proteinuria disappear in 2 weeks in 80% of children. In 10% of cases, proteinuria and haematuria persist for a long time. Five per cent of cases suffer from complications. (Few suffer from RPGN.)

Poor prognosis is seen in children with prolonged oliguria and azotaemia.

NEPHROTIC SYNDROME

Nephrotic syndrome is a clinical state characterised by the following features:

- Proteinuria—massive (>40 mg/m^2/hour or spot protein to creatinine ratio >3 mg/mg)
- Hypoproteinaemia—albumin <2.5 g/dL
- Generalised oedema—gross oedema

Hypercholesterolaemia (>220 mg/dL) is often associated.

PATHOGENESIS

The patients with nephrotic syndrome have an inherent susceptibility to develop T-cell dysfunction. The released lymphokine (IL-2) causes a decrease in the heparan sulphate sialoprotein and hence the anionic charge of the glomerular basement membrane (GBM). This leads to massive proteinuria. For details see Fig. 12.1.

CLASSIFICATION

Classification According to Age

1. Congenital nephrotic syndrome—presents at birth or before 3 months of life (Fig. 12.2)
   - Primary type has a known inheritance pattern and can be of Finnish type or non-Finnish type. It carries poor prognosis
   - Secondary to in utero infections such as congenital syphilis, toxoplasmosis and CMV disease. It is less common
2. Infantile nephrotic syndrome—onset between 3 months and 1 year of age
3. Childhood nephrotic syndrome—onset between 2 and 8 years
4. Adult (pubertal)

The classification according to age is important as the response to therapy, the course of the disease

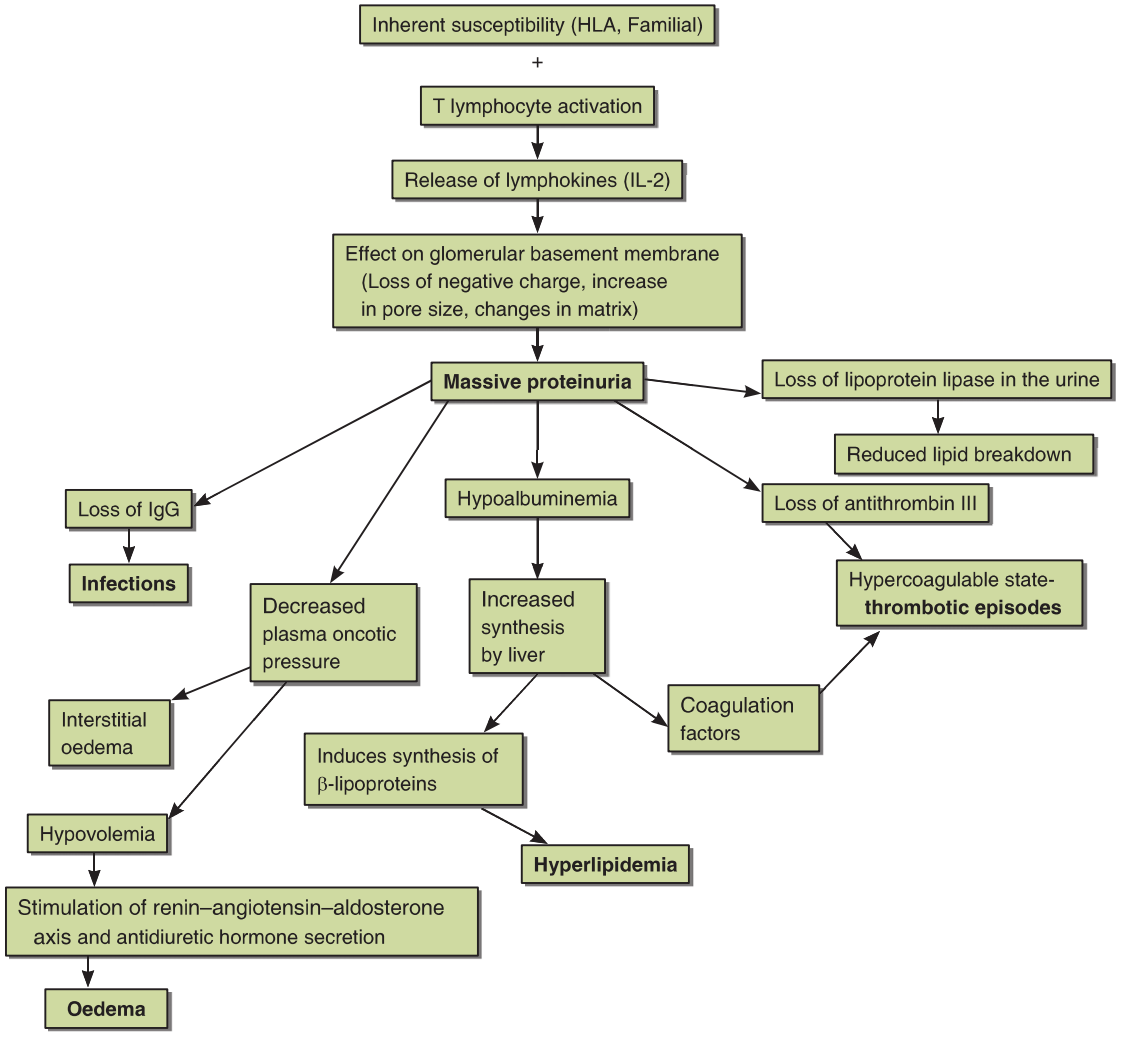


FIGURE 12.1 Pathogenesis of nephrotic syndrome.



FIGURE 12.2 Congenital nephrotic syndrome. Note the puffiness of face, ascites and pedal oedema.

and the final outcome varies according to the age of onset. The differences between congenital and infantile nephrotic syndromes are given in Table 12.11.

Etiological Classification

Classification of nephrotic syndrome according to aetiology is as follows:

1. Primary nephrotic syndrome—idiopathic, responsible for about 90% of cases of childhood nephrotic syndrome

TABLE 12.11 Differences between Congenital and Infantile Nephrotic Syndromes

Features	Congenital	Infantile
Family history	Positive	Negative
Age of onset	Usually begins at <3 months	Late onset
Placenta	Large	Normal
Complement/antibody	Reduced compliment and elevated IgM	Normal compliment and normal IgM
Histological findings	Minimal change/tubular changes	Variable
Causes	Congenital infections such as syphilis, cytomegalovirus, toxoplasmosis, rubella and malaria	Idiopathic Infections Drugs Malignancies
Prognosis	Bad (often fatal)	Depends on the cause

2. Secondary nephrotic syndrome—causes are amyloidosis, vasculitis, SLE, postinfectious glomerulonephritis and hepatitis B nephropathy (Table 12.12)

Histological Classification

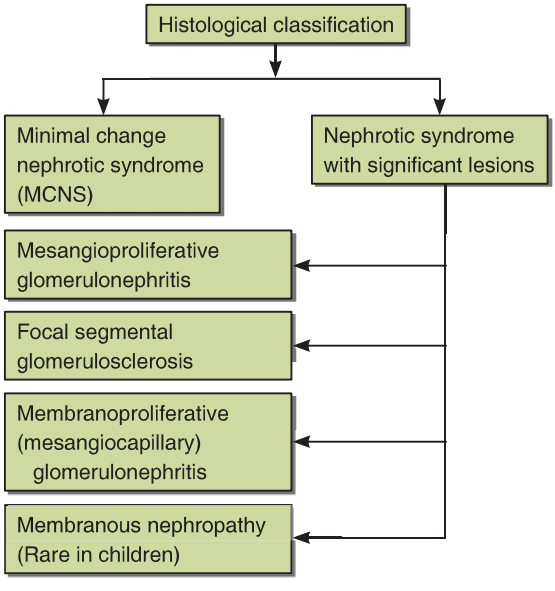


TABLE 12.12 Secondary Causes of Nephrotic Syndrome

Causes	Condition
Infections—postinfectious	Spirochetes—syphilis Viral • Hepatitis B and C infection • HIV type I Protozoa—plasmodium malaria and toxoplasmosis
Malignancy	Lymphoma—Hodgkin's disease (results in MCNS) Leukaemia
Drugs	Gold Penicillamine NSAIDs Mercury α-Interferon Lithium Heroin
Hereditary	Congenital nephrotic syndrome HSP Hereditary nephritis
Endocrine	Diabetes mellitus
Multisystem disorders	Systemic lupus erythematosus Collagen vascular disorders Polyarteritis nodosa Vasculitis due to any cause
Miscellaneous	Insect bites—bee sting Food allergens Amyloidosis Sjogren's syndrome

MINIMAL CHANGE NEPHROTIC SYNDROME

Minimal change nephrotic syndrome (MCNS) is most commonly seen in 85% of all cases of nephrotic syndrome in children.

- Age group—2–6 years
- Gender—ratio of affected males to females 2:1
- Aetiology is not known; immunological aetiology may be the cause, as this condition responds to steroids

Clinical Features

Onset of MCNS is insidious. The symptoms usually follow an upper respiratory infection. The oedema

progresses gradually in the following manner:

1. Puffiness of face due to oedema around the eyes
2. Oedema of the legs (fast oedema <20 seconds)
3. Generalised oedema (ascites, hydrothorax and scrotal oedema in male children) (Fig. 12.3)

Look for associated infections. Blood pressure is normal in cases with MCNS.

Investigations

1. Urine—heavy proteinuria (3+ to 4+)
2. Blood urea and creatinine usually normal; no azotaemia
3. Serum albumin—low
4. Complement levels normal

NEPHROTIC SYNDROME WITH SIGNIFICANT LESIONS

Nephrotic syndrome with significant glomerular lesions accounts for about 15% of cases.

- Age group—occurs at any age but usually affects older children.
- Pathological changes seen are focal segmental glomerulosclerosis (FSGN) (about 10%), mesangioproliferative (about 5%) and membranoproliferative glomerulonephritis (MPGN) (rare).

Clinical Features

1. Generalised oedema with its typical pattern of progression.
2. Macroscopic haematuria may be present.
3. Blood pressure may be elevated in patients with significant glomerular lesions.
4. Nephrotic syndrome with significant lesions should be suspected when any of the following features is seen:
   - Age more than 8 years
   - Hypertension
   - Haematuria
   - Renal dysfunction
   - Extrarenal symptoms
   - Rash
   - Arthralgia
   - Fever
   - Decreased serum compliment levels

Investigations

- Azotaemia



(a)



(b)

FIGURE 12.3 Nephrotic syndrome. (a) Note that the child has normal sensorium and puffiness of face. (b) Note the transverse stretching of umbilicus due to ascites and scrotal oedema.

- Hypocomplementaemia

Table 12.13 compares the characteristic features of MCNS and NS with significant lesions.

ASSOCIATED DISEASES

Some other diseases are often seen in association with nephrotic syndrome. They should be suspected in the presence of following clinical findings:

- Generalised lymphadenopathy—leukaemia and lymphoma
- Dysmorphism–Alport syndrome
- Skin—purpura in HSP; maculopapular rash in vasculitis due to any cause
- Joint (arthritis)— SLE, HSP and rheumatoid arthritis
- Abdomen (hepatosplenomegaly)—malaria and syphilis

COMPLICATIONS

Complications can be due to the disease itself or due to the drugs that are used in nephrotic syndrome. The chief complication of nephrotic syndrome is the infection followed by thrombotic complications.

Complications Due to the Disease

1. Oedema—due to loss of proteins
2. Anaemia—due to loss of transferrin
3. Hypothyroidism—due to loss of thyroid-binding globulin
4. Hypocalcaemia—due to loss of vitamin

TABLE 12.13 Characteristic Features of MCNS and with Significant Glomerular Lesions

No.	Features	Minimal Change Glomerular Lesions	Significant Glomerular Lesions
1	Incidence (%)	>85	<15
2	Age of onset (years)	2–6	<2 or >6
3	Sex incidence	Boys > girls	M = F
4	Haematuria	Rare	Haematuria or microscopic haematuria common
5	Hypertension	Rare	Common
6	Glomerular filtration rate	Normal	Decreased or normal
7	Renal lesions	Normal or minimal change	Significant lesions such as mesangial proliferation, mesangiocapillary and membranoproliferative focal glomerulosclerosis
8	Pathologic abnormality	Loss of negatively charged glycoproteins and proteoglycans from the basement membrane	Deposition of immune complexes in the glomeruli and activation of the compliments
9	Renal biopsy • Light microscopy • Immunofluorescent examination	 Loss of epithelial foot process Negative; occasionally mesangial IgM deposits	 Mild to severe abnormalities Immunoglobulin and C_3 complement often present
10	Serum complement serum C_3	Normal range	Decreased in some Low in MPGN
11	Selectivity of proteinuria	Urine consists mainly of albumin; high selectivity	Large molecular weight proteins are also present in urine; low selectivity
12	Response to corticosteroids	Remission in >95% of MCNS	Proteinuria persists in most of the patients
13	Other drugs	Not needed	Antimetabolites such as cyclophosphamide, chlorambucil and cyclosporine-A are indicated
14	Complications such as renal failure	Not common	Common
15	Prognosis	Good; relapses stop by second decade	Fair-to-poor variable progression of renal damage

D–binding globulin and loss of 1,25, dihydroxy cholecalciferol

5. Infections—due to *Streptococcus pneumoniae*, gram-negative organisms and varicella are common. Children usually present with subacute bacterial peritonitis, pneumonia, cellulitis and upper respiratory tract viral infections. Factors predisposing to infections are as follows:
   - Loss of immunoglobulin
   - Decreased cell-mediated immunity
   - Treatment with steroids
   - Presence of oedema

   Immunisation with pneumococcal and varicella vaccines is recommended once the patient is off steroid therapy
6. Thromboembolism—predisposition to renal vein thrombosis, peripheral vein thrombosis and cerebral vein thrombosis. Arterial thrombosis occurs in the pulmonary artery. Predisposing factors are immobilisation, hypovolaemia, use of diuretics, venepuncture and infections. Causes are as follows:
   - Loss of anticoagulation factors such as antithrombin III
   - Hyperfibrinogenaemia
   - Impaired fibrinolysis
   - Reduced activity of protein C and protein S
   - Enhanced platelet aggregation
7. Renal failure
   - Acute renal failure—occurs due to hypovolaemia and diuresis
   - Chronic renal failure
8. Convulsions may occur due to the following causes:
   - Hypocalcaemia
   - Hypertension
   - Renal failure
   - Hyponatraemia
   - Cerebral vein thrombosis
9. Pericardial effusion and hydrothorax—due to fluid retention
10. Postural hypotension may be due to hypovolaemia
11. Accelerated atherosclerosis can occur
12. Zinc and copper deficiency states due to loss of metal-binding proteins
13. 25(OH) vitamin D low; vitamin D-binding protein is lost in the urine

Complications Due to Drugs

1. Steroids
   - Cushingoid facies
   - Ocular—subcapsular cataract and glaucoma
   - Infections, striae and thinning of skin
   - Musculoskeletal—short stature (delayed bone age), steroid-induced osteopenia, aseptic necrosis of femoral head and myopathy
   - Gastrointestinal—gastritis/peptic ulcer, GI bleeding and pancreatitis
   - Central nervous system—pseudotumour cerebri, depression, psychosis and irritability
   - Endocrinal—suppression of hypophyseal pituitary adrenal axis
   - Metabolic—diabetes and hyperlipidaemia
   - Renal—nephrocalcinosis and hypertension
2. Cyclophosphamide—haemorrhagic cystitis, bone marrow depression, alopecia, risk of secondary malignancy and gonadal toxicity. The latter leads to sterility in males.
3. Furosemide—hypokalaemia, hyponatraemia, hyperuricaemia, hypercalciuria, hypocalcaemia, hypovolaemia, tinnitus, deafness and acute interstitial nephritis

INVESTIGATIONS

Investigations for Diagnosis

Urine Examination

1. Macroscopic and microscopic examination
   - Hyaline casts are present in MCNS and granular casts are present in nephrotic syndrome with significant glomerular changes.
   - Urine for RBCs is usually negative in MCNS. It is positive in nephrotic syndrome with significant lesions.
2. Urine for proteins
   - Heavy proteinuria (3+ or 4+). Tests used for proteinuria are heat coagulation test, Heller's test and Dipstick test.

TABLE 12.14 Grades of Proteinuria on the Basis of Urinary Protein Value

Severity of Proteinuria	Urinary Protein (mg/1.73 m²/day)
Mild	150–500
Moderate	500–1700
Severe	>1700

- Twenty-four-hour urinary protein is increased. Normal proteinuria is less than 150 mg/day (Table 12.14). Of this, albumin consists of <30 mg/day and the remaining is Tamm horsfall protein (a mucoprotein).

3. Selective proteinuria—It is the ratio of clearance of the high-molecular-weight proteins (e.g. IgG) to low-molecular-weight proteins (e.g. transferrin and albumin). Low ratio indicates highly selective proteinuria, which is seen in MCNS. High ratio is seen in nephrotic syndrome with significant lesions.
4. Urine spot protein-creatinine ratio—This ratio is more than 3.

Blood Examination

1. Serum proteins—decreased
   - Total serum proteins—decreased
   - Albumin/globulin ratio—reversed
   - IgG levels—decreased
   - IgM levels—increased
2. Lipid profile
   - Serum cholesterol—elevated
   - VLDL and LDL—increased
   - HDL—normal, increased or decreased
3. Serum complement level
   - C_3 levels—normal
   - Hypocomplementaemia will be seen in SLE and MPGN
4. Serum protein electrophoresis
   - Albumin and α_1-globulin—decreased
   - α_2-globulin and β-globulin—elevated
   - Fibrinogen—elevated

Investigations for Aetiological Factors

1. Hepatitis B surface antigen (HBsAg)
2. Antinuclear antibodies
3. Antistreptolysin O titres
4. Mantoux test (to rule out tuberculous infection predisposing to amyloidosis, which can cause nephrotic syndrome)
5. Coomb's test—positive in SLE

Investigations for Complications

1. Blood count, Hb%—anaemia
2. Total and differential count—leucocytosis is seen in infections
3. Peripheral smear—RBCs show normocytic normochromic anaemia in HSP. Haemolytic anaemia is seen in renal vein thrombosis and HSP
4. Blood urea and creatinine are normal usually but may be elevated in the presence of severe hypovolaemia and decreased renal perfusion
5. Serum calcium may be decreased
6. Urine culture and sensitivity tests are done to rule out UTIs
7. X-ray chest—bilateral pleural fluid
8. Ultrasonogram of abdomen—look for ascites
9. Renal biopsy—in cases with lesions other than MCNS, the renal biopsy helps in establishing histopathological diagnosis. The changes seen in renal biopsy include FSGN, mesangioproliferative glomerulonephritis, MPGN. Indications for renal biopsy are as follows:

   (a) At the onset of nephrotic syndrome
   - Age of onset below 1 year and above 8 years—non-MCNS are common after 7–8 years of age
   - Persistent haematuria (microscopic or gross)
   - Secondary nephrotic syndrome (SLE and HSP)
   - Persistently low C_3
   - Hypertension—sustained
   - Renal failure not due to hypovolaemia
   - Systemic disease
   - Family history of renal disease

   (b) After the initiation of treatment
   - To evaluate the efficacy of treatment
   - To detect the transformation of MCNS to significant changes like FSGN

- Patients not responding to steroids
- Frequent-relapse nephrotic syndrome
- Steroid-dependent nephrotic syndrome
- Steroid-resistant nephrotic syndrome—not responding to 8 weeks of prednisolone according to the International Study for Kidney Diseases in Children (ISKDC)

(c) Other indications for renal biopsy are kidney biopsy prior to initiation of cytotoxic therapy. Annual kidney biopsy is indicated during the therapy because renal biopsy is a better indicator of renal damage than GFR

TREATMENT

Salt Restriction

It is important to decrease the oedema. No added salt (500 mg/day) should be advised in the diet until oedema subsides. Salt-free or unsalted diet does not mean sodium free. It means that no sodium is added; the food itself may contain sodium.

Ordinary table salt (sodium chloride) is 40% sodium and 60% chloride. Sodium is absolutely essential for life, playing a crucial role in the regulation of body fluids and blood pressure. Unfortunately, most of us consume more sodium than we need through processed foods, snacks and junk foods. A single teaspoon of table salt contains an entire day's recommended intake of sodium.

'Low sodium' label on a food item means that the food item contains 140 mg less of sodium per serving. 'Reduced sodium' means that the product has 25% less sodium than the regular items.

The foods labelled 'very low sodium' will contain 35 mg or less of sodium per serving, While those labelled 'sodium free' will contain less than 5 mg per serving.

Fluid Restriction

Total fluid intake should be restricted to the urine output plus insensible fluid loss.

Insensible fluid loss is the amount of fluid lost through the skin and respiratory tract. It is calculated as 30 mL/kg in young children and 20 mL/kg in older children.

Diet

Normal protein intake of 1.5–2 g/kg/day is recommended. High protein intake should not be advised, as this will cause increased filtration of proteins in the glomerulus, resulting in glomerulosclerosis and renal failure. High protein intake in the range of 3–5 g/kg/day is recommended if the nephrotic syndrome is associated with malnutrition. Calorie intake should be decreased in acute phase. Fat intake should be avoided. Foods that can be advised are idly, idiappam with sugar, egg white, rice kanji, and curd rice. Foods such as pickles, chips and banana should be avoided.

Drug Therapy for Proteinuria

Steroids

Steroids should be started immediately after infections have been ruled out.

Start prednisolone 2 mg/kg for 4 weeks. Then taper the dose, depending on the response to the treatment. After 4 weeks, if proteinuria is present, continue the same dose of prednisolone for the next 4 weeks. If proteinuria has decreased, give the prednisolone on alternate days for the next 4 weeks. Then slowly taper the dose of steroids.

For relapse cases, patient should be treated with daily doses of prednisolone same as above till the remission occurs. After remission the therapy is changed to alternate-day dosing for 1–2 months.

Though prednisolone is the drug of choice, a new steroid derivative, deflazacort (a heterocyclic synthetic oxazoline glucocorticoid) has been found useful in treating steroid-sensitive nephrotic syndrome. This drug has the same therapeutic effect as that of prednisolone, but lower side effects and higher remission rate.

APN regimen. *Arbeitsgemeinschaft fur Padiatrische Nephrologie regimen*, 1988.

1. Initial episode—prednisolone 60 mg/m^2/day (or 2 mg/kg/day) should be given daily for 6 weeks in two or three divided doses, followed by 40 mg/m^2/day (1.5 mg/kg/day) on alternate days for 6 weeks.
2. Relapse—prednisolone 60 mg/m^2/day should be given till remission, followed by 40 mg/m^2/day for 3 days in a week for 6 weeks.

Modified APN regimen. Tablet prednisolone 2 mg/kg/day for 6 weeks, followed by 2 mg/kg/day on alternate days for 6 weeks.

ISKDC regimen. International Study Group on Kidney Disease in Children regimen.

1. Initial episode—prednisolone 60 mg/m^2/day (or 2 mg/kg/day) should be administered in 2–3 divided doses for 4 weeks, followed by 40 mg/m^2/day (1.5 mg/kg/day) daily for 3 consecutive days in a week for 4 consecutive weeks. After this steroid treatment is stopped without tapering. Response occurs in 2 weeks with disappearance of proteinuria.

Duration (weeks)	Response
2–3	Proteinuria disappears
8–12	Serum albumin and cholesterol return to normal

2. Relapse—treatment is the same as for the initial attack, except that prednisone is given at a dose of 60 mg/m^2/day till the urine has been free of protein for 3 consecutive days.

Modified ISKDC regimen. After 4 weeks of treatment, prednisolone 40 mg/m^2 is given as a single morning dose on alternate days for 4 weeks, rather than on 3 consecutive days of each week.

Alternative Therapy

If the child is resistant to steroids, alternative modalities of treatment can be started either alone or in combination with steroids. Indications are as follows:

- Frequent relapse
- Steroid resistant
- Steroid dependent

Most of the immunomodulant, immunostimulatory and cytotoxic drugs are useful in children older than 6 years, with the duration of the disease more than 2 years. In some steroid-resistant cases, remission induced by the cyclophosphamide or cyclosporine-A results in a subsequent steroid-responsive state.

Immunosuppressants

1. Steroids (high doses)—intravenous methyl prednisolone is given in a dose of 30 mg/kg as multiple infusions at increasing intervals over a period of 18–20 months. Initially this is given twice a week, then twice a month and then monthly
2. Cyclophosphamide
   (a) Dose—2 mg/kg/day
   (b) Duration—8–12 weeks
   (c) Contraindications
      - Infection
      - White blood cell counts <5000/mm^3
3. Chlorambucil
   (a) Dose—0.2–0.3 mg/kg/day
   (b) Duration—12 weeks
4. Aggressive triple therapy for steroid-resistant cases—intravenous methyl prednisolone along with prednisolone and cyclophosphamide on alternate days

Immunomodulants/Immunostimulants. Levamisole is given in a dose of 2–2.5 mg/kg on alternate days for 6–36 months. Best results are obtained when this drug is introduced during the phase of steroid-induced remission, while the steroid dose is being tapered.

Anticoagulants. Heparin is used as an anticoagulant.

Cyclosporine-A. It is given when patients have not responded to levamisole and cyclophosphamide. This drug has an inhibitory effect on the synthesis of IL-2 by the activated T-lymphocytes. The recommended dose is 4–6 mg/kg/day orally for 1–2 years. This drug is useful in steroid-responsive, frequently relapsing nephrotic syndrome or steroid-dependent nephrotic syndrome. Cost of the treatment, maintaining the serum levels between 60 and 160 mg/dL and serious side effects such as nephrotoxicity restrict the use of this drug. Indications for using cyclosporine-A are as follows:

- Steroid-induced complications
- Steroid- and cyclophosphamide-resistant nephrotic syndrome

Other Drugs that Reduce Proteinuria. Patients who does not respond to these treatments or develop severe toxicity can be treated with drugs that reduce

proteinuria. Indomethacin was used, but it is highly toxic and can lead to renal failure.

1. Angiotensin-converting enzyme (ACE) inhibitors: These reduce proteinuria by their effect on efferent arterioles in reducing intraglomerular and filtration pressures. Direct effect on the basement membrane permeability to protein is also seen. These drugs cause alteration in the capillary permeability and reduction in the glomerular hydrostatic pressure. This reduction on proteinuria results in an increase in the serum albumin levels and a reduction in oedema
   - Captopril 0.25–0.5 mg/kg/day
   - Enalapril 0.1–0.2 mg/kg/day
   - Losartan 0.5 mg/kg/day
2. Antiplatelet drugs
   - Dipyridamole
   - Aspirin (low dose)—this is used as an adjuvant therapy in preventing progressive renal damage in chronic glomerulonephritis with nephrotic syndrome

Hypercholesterolaemia

This can be treated by HMG coenzyme reductase inhibitor (lovastatins), which decreases the cholesterol levels in the blood.

MONITORING

- Weight monitoring
- Intake or output monitoring
- Urine albumin chart
- Abdominal girth measurement—needed if ascites is present. The abdominal girth at the level of umbilicus should be measured daily

RESPONSE TO TREATMENT

The child with nephrotic syndrome may show response in any of the ways shown in Table 12.15.

TABLE 12.15 Criteria for Responses to Treatment of Nephrotic Syndrome

Response to Treatment	Criteria
Remission	Urinary protein excretion <4 mg/m²/hour; nil or trace by dipstick on spot sample for 3 consecutive days Serum albumin more than 3.5 g/dL No oedema
Relapse	Urine albumin ≥3+ by dipstick for 3 consecutive days Proteinuria >40 mg/m²/hour for three consecutive specimens
Frequent relapse	Two or more episodes in 6 months of initial response Four or more episodes in any 12-month period
Infrequent relapse	Less than three episodes in 12 months Less than two episodes in 6 months
Steroid sensitive (steroid responsive)	Disappearance of proteinuria and all clinical and biochemical features within 8 weeks of starting a standard course of steroid therapy
Steroid resistance	Failure to achieve remission after 4 weeks of daily therapy with oral prednisolone at a dose of 2 mg/kg/day Persistent proteinuria after completion of treatment
Steroid-dependent cases	Occurrence of two consecutive relapses during steroid therapy or within 2 weeks of its cessation Relapse after stopping the drugs

TREATMENT OF COMPLICATIONS

1. Oedema
   - Diuretics are indicated if the oedema is severe and associated with massive ascites. Furosemide is given in a dose of 2 mg/kg. For the treatment of refractory oedema, give furosemide 2 mg/kg and hydrochlorothiazide 4 mg/kg.
   - Intravenous infusion of 20% albumin 1 g/kg over 1–4 hours with furosemide 2 mg/kg may be given if the serum albumin is low and associated with decreased renal perfusion and oliguria. The effect will be transient. Complications such as pulmonary oedema and CCF may occur.
   - Ultrafiltration.
   - Head-out water immersion, where the child sits or stands in a water tub with the head

kept out of the water. Owing to the hydrostatic pressure, there is increased venous return. The atrial dilatation results in atrial natriuretic peptide secretion, which results in natriuresis and diuresis.
- Restriction of water intake to insensible water loss plus urine output.

2. Associated infections such as peritonitis, pneumonia, urinary tract infections and cellulitis should be treated with appropriate antibiotics.
3. Anaemia—blood transfusion or preferably packed cell transfusion can be given in the presence of anaemia.
4. Renal vein thrombosis—long-term anticoagulants are indicated in renal vein thrombosis.
5. Renal failure—dialysis is indicated in case of renal failure.
6. Ascitic fluid or hydrothorax—paracentesis of ascitic fluid or hydrothorax may be indicated if these cause pressure symptoms.

As this is a chronic disorder and there is a possibility of recurrence, emotional and psychological support for both the child and the parents should be given.

PROGNOSIS

Eighty-five per cent of the nephrotic syndrome cases respond to steroids. Five per cent of cases recover spontaneously; 10% cases are steroid resistant. Ninety-five per cent of the children with MCNS will respond to prednisolone with diuresis, loss of oedema and decrease in proteinuria by 14 days. In cases with significant lesions, one-third recover completely and one-third of the cases have CRF. The prognosis is poor for the remaining children.

Of all the cases of nephrotic syndrome, 20% suffer from one episode with no further disease activity after first year, 45% have relapsing disease with ultimate cure, 10% have relapsing disease with continued disease activity for 10 years or more and 15% have relapsing disease with death. Remaining 10% die within 2 years of onset. Survival rate in relation to time from diagnosis is given in Table 12.16.

Differentiating features between AGN and nephrotic syndrome are shown in Table 12.17.

TABLE 12.16 Survival Rate in Relation to Time from Diagnosis

Time from Diagnosis (Years)	Survival Rate (%)
1	94
2	90
5	85
10	79
15	77

TABLE 12.17 Differentiating Features between AGN and Nephrotic Syndrome

	AGN	Nephrotic Syndrome
Features		
Age group	Older children, 4–10 years	2–6 years
Preceding illness Skin/throat infections impetigo	Usually present	Not associated
Pathogenesis	Immune complex	Minimal—T-cell dysfunction
Onset	Acute	Insidious
Haematuria	Positive	Negative
Features of CCF	Positive	Negative
Head ache	Present	Not present
Convulsions	Present	Not present
Hypertension	Present	Not present
Oedema	+ Mild oedema	+++ Massive oedema
Recurrence	Not seen—rare	Present
Investigations		
Urine	RBC casts, granular casts, haematuria and oliguria	Fat-laden cells
Albuminuria	Moderate	Massive
Serum cholesterol	Normal	Increased
Haemoglobin	Haemoconcentration	Decreased due to haemodilution

NEPHRITIC–NEPHROTIC SYNDROME

Primary glomerular diseases can present as acute nephritic syndrome in some children and nephrotic syndrome in others, with some exceptions, for example minimal change disease always produces nephrotic syndrome and crescentic nephritis always manifests as nephritic syndrome. MPGN presents as nephritic syndromes in 15%–20% and nephrotic syndrome in 60% of patients. Some cases may present as acute nephritic syndrome but may turn out to be a nephrotic syndrome on evaluation.

CHAPTER 13

Blood Disorders

Whole blood contains three types of blood cells, namely red blood cells, white blood cells and platelets. In small infants, the production of these blood cells occurs in the bone marrow throughout the body. With advancing age, the production gets confined to the bone marrow of the vertebrae, ribs, pelvis, skull, sternum and parts of the humerus and femur. Blood disorders affect the production of blood and its components such as blood cells, blood proteins, haemoglobin, coagulation factors, etc.

HISTORY TAKING

Age

- Nutritional anaemia is not common under the age of 6 months in breastfed infants.
- Thalassaemia presents in late infancy (after 6 months) due to the presence of foetal haemoglobin (HbF).
- Fanconi's anaemia usually presents at the age of 6–8 years.
- Sickle-cell anaemia presents by 2–4 months of age.

Sex

X-linked disorders such as glucose-6-phosphate dehydrogenase (G6PD) deficiency and haemophilia are common in males.

Place

- Sickle-cell anaemia is common in hilly areas and tribal communities such as those in Chhatisgarh.
- Thalassaemia is more common in Gujarat and Maharashtra.

Presenting Complaints

Following are the usual presenting complaints:

- Easy fatigability on exertion
- Breathlessness (due to anaemia)
- Pallor
- Bleeding from injured sites, spontaneous bleeding

History of Present Illness

- Non-specific symptoms—tiredness, breathlessness, lassitude, pallor, palpitation
- GI bleeds—haematemesis (vomiting of fresh blood), melaena (passage of black tarry stools), haematochezia (passing frank blood per rectum). Ask about number of episodes, major/minor, tolerated/not tolerated. Also enquire about the onset (rapid/slow), frequency of the bleeds, bouts in each episode, precipitating factors. For details, see chapter on abdomen history taking
- Diarrhoea—malabsorption, inflammatory bowel disease

- H/o bone pain (leukaemia)
- H/o pain in abdomen (worm colic, lead poisoning which is associated with hypochromic microcytic anaemia)
- H/o abdominal pain, pain in the limbs, headache, convulsions, hemiplegia and psychic changes (due to vaso-occlusive crisis in sickle-cell anaemia)
- H/o fever—high/low grade, associated with chills and rigors (malaria). Salmonella infection is common in sickle-cell anaemia
- H/o haematuria, dark-coloured urine (in blackwater fever, malaria), yellow-coloured urine (jaundice)
- H/o pica (associated with iron deficiency anaemia, worm infestations, lead poisoning)
- H/o constipation—symptoms of hypothyroidism (anaemia)
- H/o arthritis and arthralgia
- H/o passing worms in stools, vomitus (hookworms)
- H/o dyspnoea, tachypnoea, palpitations—features of congestive cardiac failure (CCF) (due to anaemia)
- H/o visual disturbances—osteopetrosis

History of Past Illness

- H/o jaundice (haemolytic anaemia, Wilson's disease)
- H/o gastrointestinal bleeds
- H/o infections—tuberculosis, chronic urinary tract infection (UTI) (chronic infections will be associated with anaemia)
- H/o worm infestations
- H/o prior similar illness (haemolytic anaemia)
- H/o puffiness of face (cardiac failure due to anaemia)
- H/o oedema—pedal oedema, generalised oedema (anasarca)
- H/o pica—common in severe iron deficiency anaemia and worm infestation
- H/o oliguria/anuria (renal failure)
- H/o dysentery (haemolytic uremic syndrome)

Treatment History

As various drugs can lead to suppression of the marrow function, detailed history should be taken regarding intake of drugs, which can cause marrow toxicity. Patients taking aspirin will have defective platelet functions. The following should be asked:

- H/o hospitalisation and its details—indications, nature of treatment given, duration of stay, etc.
- H/o complications such as bleeding and intake of drugs which cause bleeding—salicylates, NSAIDs.
- Drugs causing aplastic anaemia—chloramphenicol, gold salts (Table 13.1).
- Drugs causing haemolysis in G_6PD deficiency—primaquine, quinine, naphthalene, sulfonamides, probenecid, para-aminosalicylic acid, nalidixic acid.
- H/o blood transfusion—age at which first transfusion was given, indications for the transfusion, number and frequency of transfusions, interval between transfusions, route of transfusion (for example, umbilical vein in new born) etc. Also ask about complications if any and its details.
- H/o exchange transfusion—indications.
- H/o previous intestinal surgery (megaloblastic anaemia due to malabsorption or vitamin B_{12} deficiency).

TABLE 13.1 Mechanism by Which Drugs Cause Anaemia

Mechanism	Drugs
Bone marrow depression	Chloramphenicol Phenylbutazone Cyclophosphamide 5-FU
Increased destruction of RBCs	Penicillin Cephalosporins
Folate antagonists	Phenytoin

Antenatal History

- Booked case—would have received iron and folic acid
- Interval between two pregnancies—less the interval more are the chances for development of iron deficiency anaemia
- Maternal malnutrition—anaemia in mother predisposes to anaemia in the baby
- Intrauterine infection (TORCH)—fever with rash

- Did the mother receive iron and folic acid tablets?
- H/o multiple pregnancies—predispose to anaemia by twin–twin transfusion
- H/o antepartum haemorrhage

Birth History

- Mode of delivery
- Details regarding the clamping of cord, any manipulation such as milking of the cord done immediately after delivery
- Gestational age of the baby—preterm babies are more prone to develop anaemia as iron stores are replenished in the baby near term
- Low birth weight—will have decreased iron stores
- Cried soon after birth or not
- H/o bleeding from cord
- H/o birth injury resulting in bleeding

Neonatal History

- Umbilical bleeding/bleeding from other sites/internal haemorrhage/convulsions
- H/o neonatal jaundice (hereditary spherocytosis)
- Cephalhaematoma
- Weight gain of the baby

Growth and Development History

- Any delay in the milestones (motor and mental milestones are delayed in iron deficiency anaemia, megaloblastic anaemia)
- Retardation in physical growth
- Anaemia is common during the periods of rapid growth

Nutritional History

- Was the child breastfed? How long? Breast milk has iron with high bioavailability. Hence, iron deficiency anaemia is uncommon in exclusively breastfed infants before 4–6 months of age.
- When was the weaning started?
- Did the diet include iron-rich foods?
- Megaloblastic anaemia due to folic acid deficiency is seen in children who are on goat's milk.

Personal History

- Does the child have any food fads?
- Strict vegetarians are prone to develop megaloblastic anaemia due to vitamin B_{12} deficiency.

History of Allergy and Contact

- Chronic infections such as tuberculosis predispose to anaemia.
- Cow's milk protein allergy results in gastrointestinal blood loss.

Family and Sibling History

- Ask about the history of similar illness in other family members as many blood disorders are inherited. For instance, thalassaemia and sickle-cell anaemia are inherited as autosomal recessive diseases. Hereditary spherocytosis is usually inherited as autosomal dominant disorder (Table 13.2)
- H/o consanguinity (autosomal recessive disorders)
- H/o bleeding tendencies/anaemia/jaundice/gall stones/blood transfusions
- H/o splenectomy

TABLE 13.2 Mode of Inheritance of Blood Disorders

Inheritance	Conditions
Autosomal dominant	Hereditary spherocytosis
Autosomal recessive	Thalassaemia Sickle-cell anaemia
X-linked	G6PD deficiency

Environmental History

History of exposure to toxic substances and duration of such exposure should be checked. The patient should be asked if he had any contact with chemicals that could cause toxicity to the bone marrow or blood elements.

Socioeconomic History

- Low socioeconomic class and unhygienic conditions predispose to worm infestations and anaemia.

- Open air defecation predisposes to hookworm infestation.
- Source of water ponds or lakes in the vicinity may predispose to various infections and infestations.

GENERAL EXAMINATION

Look for the following features:

- Appearance—well/ill-looking, comfortable/dyspnoeic
- Consciousness—normal/altered/unconscious
- Nutritional status—well nourished/under-nourished
- Decubitus—a child with severe anaemia and cardiac failure may prefer not to lie down
- Facies—normal/dysmorphic
- Eyes—conjunctival pallor, jaundice, subconjunctival haemorrhage (Fig. 13.1)
- Oral cavity—angular stomatitis (iron deficiency anaemia, vitamin B_{12} deficiency), telangiectasia (lips), gingival hyperplasia, gum bleeds (leukaemia, thrombocytopenia), tongue colour and smoothness (tongue is smooth and red in various forms of anaemia), glossitis (vitamin B_{12} deficiency), petechiae over buccal mucosa, tonsils (size), oral thrush (leucopenia, agranulocytosis), palatal purpura (glandular fever)



FIGURE 13.1 Purpura and subconjunctival haemorrhage in a child with ITP.

- Lymph nodes—lymphadenopathy (size, number, consistency, discrete or confluent, mobile or fixed, attachment to the surrounding skin)
- Colour—pallor, plethora, jaundice (may be seen in haemolytic anaemia)
- Skin rash—purpura, petechiae, ecchymosis and bruising
- Nails—brittle nails, clubbing, koilonychias (nutritional anaemia)
- Bones and joints—sternal bony tenderness (leukaemia), joint deformities, swelling and restricted movements
- Perianal region—infections around the anus are common in leucopenia. Bleeding and haematoma may also be seen
- Signs of anaemia—pallor, koilonychia (iron deficiency anaemia), tachypnoea, raised jugular venous pressure, flow murmurs, ankle oedema, postural hypotension and tachycardia
- Features suggestive of Fanconi's anaemia—short stature, microcephaly, hyperpigmentation, absent radius, absent or bifid humerus

Some of these general examination findings and their associated conditions are given in Table 13.3.

Vital Signs

- Pulse rate increased in severe anaemia, bounding pulses due to hyperdynamic circulation
- Fever may be present in leukaemia
- Respiratory rate—tachypnoea in severe anaemia, CCF

Anthropometry

- Growth retardation is seen in chronic diseases
- Height/length—normal or decreased
- Weight may be increased (oedema), decreased (chronic anaemia, leukaemia) or normal

SYSTEMIC EXAMINATION

Abdomen

- Hepatomegaly
- Spleen absent in asplenia
- Splenomegaly in haemolytic anaemia, storage disorders, osteopetrosis

TABLE 13.3 Clinical Findings and Associated Blood Disorders

Clinical Finding		Associated Condition
Short stature		Fanconi anaemia
Head size	Microcephaly	Fanconi anaemia
	Macrocephaly	Chronic haemolytic anaemia
Facies	Frontal and parietal bossing with malar prominence	Haemolytic anaemia (thalassaemia)
	Box-like face, high arched palate, triphalangeal thumb	Diamond Blackfan syndrome
Skin	Hyperpigmentation	Megaloblastic anaemia, Fanconi anaemia, congenital dyserythropoietic anaemia
	Petechiae	Aplastic anaemia
Upper limbs	Dactylitis	Sickle-cell anaemia
	absent radius, absent or bifid humerus, absent thumb	Fanconi anaemia
	Triphalangeal thumb	Pure red cell aplasia
Eyes	Blue sclera	IDA—severe
	Microcornea	Fanconi anaemia
Tongue	Smooth, red, painful tongue	Pernicious anaemia
Nails	Koilonychia	Iron deficiency
Leg ulcers		Sickle-cell anaemia
Hepatosplenomegaly		Chronic haemolytic anaemia

- Ascites
- Inguinal and femoral lymphadenopathy

Rectal Examination

Intestinal polyps and haemorrhoids cause blood loss.

Cardiovascular System

- Haemic murmurs
- Prosthetic heart valves (causes haemolytic anaemia)
- Features of infective endocarditis

Central Nervous System

- Focal neurological deficits (haemorrhage)
- Subacute combined degeneration (vitamin B_{12} deficiency)
- Fundus examination—haemorrhage, hyperviscosity, engorged veins, papilloedema

Endocrine System

Look for features of hypothyroidism as it predisposes to anaemia.

INVESTIGATIONS

1. Complete blood count
2. Erythrocyte sedimentation rate (ESR)
3. Peripheral blood study—type of anaemia, presence of abnormal cells; sickle cells in sickle-cell anaemia, spherocytes in spherocytosis, basophilic stippling in thalassaemia and lead poisoning, target cells in iron deficiency anaemia and postsplenectomy, fragmented red blood cells (RBC) in haemolytic uremic syndrome, Heinz bodies and Howell–Jolly bodies postsplenectomy, blast cells in leukaemia.
4. Evidence of haemolysis—reticulocytosis. Polychromasia and basophil stippling are indirect evidence of reticulocytosis. Reticulocytes are identified by supravital staining with brilliant cresyl blue which stains the ribosome of the reticulocytes. It appears as reticular network. Total number of reticulocytes per 500 RBCs are counted and expressed as percentage. Reticulocytes should be corrected for the patient's haematocrit. When the patient's haematocrit or packed cell volume (PCV) is low, reticulocytes are released faster from the marrow. To adjust for this phenomenon, following formulae are useful:

$$\text{Corrected reticulocyte count (also known as reticulocyte index)} = \frac{\text{Patient's reticulocyte count} \times \text{PCV}}{45}$$

$$\text{Reticulocyte production index (RPI)} = \frac{\text{Corrected reticulocyte count}}{\text{Maturation time}}$$

Absolute reticulocyte count = Observed reticulocyte count × RBC count

Maturation time is as follows

Maturation time (days)	Haematocrit (%)
1	45
1.5	35
2	25
2.5	15

5. Red cell distribution width (RDW) (Normal 11%–15%)

   RDW = (Std. Dev. of MCV ÷ mean MCV) × 100

   If there is a large variation in red cell size, it leads to increased RDW
6. Smear for malarial parasites
7. Bleeding and clotting time
8. Partial thromboplastin time
9. Chest X-ray—for evidence of tuberculosis
10. Special investigations
    - Faecal occult blood, barium meal or enema (gastrointestinal bleeding)
    - Blood urea, creatinine (chronic renal failure)
    - Liver function tests (liver diseases)
    - Bone marrow studies—aspiration/trephine biopsy (aplastic anaemia, leukaemia, secondaries)
    - Thyroid studies—TSH, T_3, T_4.
    - Lupus erythematosus (LE) cell test (systemic lupus erythematosus [SLE])
    - Blood culture (infective endocarditis, septicaemia)

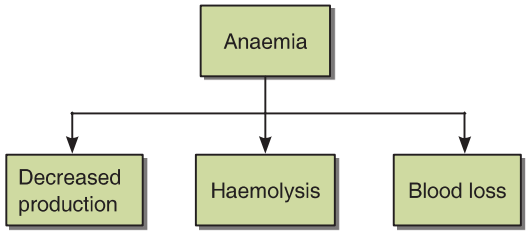
ANAEMIA

Anaemia refers to a reduction in the RBC volume. It is said to be present when the concentration of haemoglobin (Hb) in the peripheral blood is below the normal range of values for that age and sex (Table 13.4).

TABLE 13.4 Normal Range of Haemoglobin According to Age

Age Group	Normal Range (g/dL)
Cord blood	13.7–20.1
2 weeks	13.0–20.0
3 months	9.5–14.5
6 months–6 years	10.5–14.0
7–12 years	11.0–16.0
Adult female	12.0–16.0
Adult male	14.0–18.0

AETIOLOGY



Decreased Production of Erythrocytes

1. Physiologic anaemia of infancy
2. Hypoplastic and aplastic anaemia
   - Congenital hypoplastic anaemia
   - Transient erythroblastopenia of childhood
   - Fanconi's anaemia
   - Osteopetrosis—marble bone disease
   - Aplastic crisis in haemolytic anaemia
   - Aplastic anaemias
3. Deficiency of specific factors
   - Iron deficiency
   - Copper deficiency
   - Megaloblastic anaemia—deficiency of vitamin B_{12}, deficiency of folic acid
   - Pyridoxine deficiency

4. Impaired erythropoietin production
   - Anaemia in chronic diseases—chronic renal disease
   - Hypothyroidism
   - Chronic inflammatory diseases
   - Severe protein energy malnutrition
5. Marrow displacement
   - Leukaemia
   - Neuroblastoma
   - Granuloma
   - Gaucher's disease
6. Congestive splenomegaly, Gaucher's disease and other causes of splenomegaly
7. Lead poisoning
8. Acute infection or inflammation
9. Haemophagocytic syndrome
10. Sideroblastic anaemias
11. Congenital atransferrinemia

Hemolysis

Haemolytic anaemia occurs due to increased destruction or shortened lifespan of erythrocytes. The normal lifespan of the RBCs is about 120 days. The RBCs are destroyed earlier due to certain intrinsic defects. These defects may be congenital or acquired.

1. Intrinsic defects
   (a) Erythrocyte membrane defects
   - Hereditary spherocytosis
   - Hereditary elliptocytosis
   - Infantile pyknocytosis, pyropoikilocytosis
   - Hereditary stomatocytosis
   - Paroxysmal nocturnal haemoglobinuria
   - Erythropoietic porphyria
   - Abetalipoproteinemia

   (b) Haemoglobinopathies (abnormal Hb structure)
   - Sickle-cell Hb disorders
   - Thalassaemia syndromes
   - Unstable Hbs
   - Hereditary persistence of HbF

   (c) Enzymatic defects—Can be hereditary or acquired. Acquired defects can be drug induced or due to ingestion of Fava beans (Favism). Hereditary defects include
   - Defects of the Embden–Meyerhof or anaerobic pathway—pyruvate kinase deficiency, glucosephosphate isomerase, hexokinase, phosphofructokinase, etc.
   - Defects of the oxidative hexose monophospate pathway—G_6PD deficiency, glutathione reductase, glutathione peroxidase, etc.
   - Nonglycolytic enzyme deficiencies—abnormalities of erythrocyte nucleotide metabolism due to deficiency of adenylate kinase, pyrimidine 5 nucleotidase
2. Extracorpuscular mechanisms
   (a) Immune haemolytic anaemia
   - Autoimmune (warm and cold antibodies)
   - Isoimmune—haemolytic disease of newborn due to Rh incompatibility, ABO incompatibility, minor group incompatibility
   - Drug induced
   - Secondary to immune-mediated diseases such as sarcoidosis, rheumatoid arthritis, SLE, cirrhosis, infectious mononucleosis, haemolytic uremic syndrome

   (b) Non-immune haemolytic anaemia
   - Drugs/antibiotics/chemicals
   - Poisons—snake venom, lead poisoning
   - Mechanical injury—cardiac prosthesis; microangiopathy (haemolytic uremic syndrome, disseminated intravascular coagulation); march haemoglobinuria
   - Thermal injury
   - Renal disease/liver disease/Wilson's disease
   - Infections—*Clostridium welchii*, malaria, viral hepatitis, etc.

Blood Loss

It may be acute or chronic. Acute blood loss results in sudden onset of severe anaemia. In chronic blood loss, there is compensatory increase in production of red blood cells.

CLASSIFICATION

Anaemia is classified into the following types on the basis of morphology of RBCs:

1. Microcytic anaemia
2. Normocytic anaemia
3. Macrocytic anaemia (Table 13.5)

PATHOPHYSIOLOGY

Tissue hypoxia occurs due to decreased oxygen-carrying capacity by the blood as a result of decreased Hb levels. The clinical features in anaemia are due to tissue hypoxia and its consequences.

COMPENSATORY ADJUSTMENTS

Various compensatory mechanisms develop in the body to meet the oxygen requirement of the tissues. These result in increased blood flow to the tissues and increased release of oxygen from Hb. There is also decrease in physical activity by children so that their oxygen requirements are low. These mechanisms are as follows:

- Increased 2,3-diphosphoglycerate (2,3-DPG) combines with Hb and decreases the affinity of Hb to oxygen.
- The heart rate increases so that more volume of blood flows to supply more oxygen.
- Increase in cardiac output by increase in the stroke volume.
- Expansion of blood volume to maintain the total blood volume. When there is blood loss, fluid from the tissue spaces shifts to the intravascular compartment.
- Redistribution of blood flow from tissues with lower oxygen requirements, such as skin, to tissues with higher oxygen requirements such as brain and heart.

TABLE 13.5 Morphological Classification of Anaemia

Type	Investigation	Conditions
Microcytic	Ferritin decreased	IDA
	Ferritin normal/ increased	Thalassaemia Haemoglobinopathies Sideroblastic anaemia
Normocytic	Reticulocyte count decreased	Bone marrow hypoplasia Red cell dysplasia
	Reticulocyte count normal/ increased	Haemorrhage/acute blood loss Haemolytic anaemias—congenital or acquired Secondary anaemia (anaemia due to acute infections such as malaria)
Macrocytic	Megaloblastic	Vitamin B_{12} deficiency Folate deficiency
	Non-megaloblastic	Liver disorders Thyroid disorders Congenital dyserythropoietic anaemia

CLINICAL FEATURES

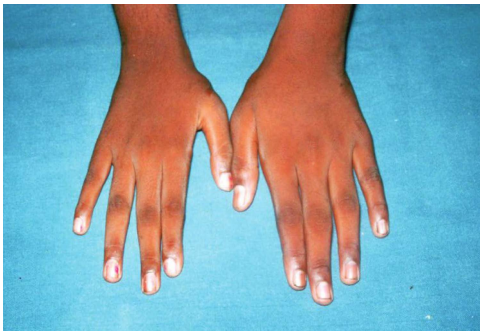
Symptoms

Tiredness, lassitude, easy fatigability, muscle weakness, poor feeding, irritability, poor school performance, dyspnoea on exertion and palpitations are common symptoms.

Signs

Pallor can be noted in the skin, oral mucosa, palmar creases, nails, skin and conjunctivae (Figs. 13.2 and 13.3). Effects of anaemia on various systems in the body are as follows:

1. Cardiovascular system—effects are due to hyperdynamic circulation and other haemodynamic changes
   - Raised jugular venous pressure (JVP)
   - CCF can occur in severe anaemia
   - Haemic murmur can be heard during mid-systole both at the apex and base of the heart. They are more common in the pulmonary area



(a)



(b)

FIGURE 13.2 Pallor due to anaemia in nails.



FIGURE 13.3 Pallor due to anaemia in palmar creases.

- Severe anaemia may present with cardiomegaly
- Decreased oxygen supply to the myocardium may result in angina

TABLE 13.6 Associated Clinical Features in Anaemia and Their Likely Causative Condition

Clinical Feature	Causative Condition
Gum bleeding, bone pain or tenderness, lymph node enlargement	Leukaemia
Bleeding tendencies	Blood loss anaemia
Leg ulcers	Sickle-cell anaemia
Peripheral neuritis	Vitamin B_{12} deficiency

2. Central nervous system—faintness, headache, lack of concentration, tinnitus, dizziness
3. Gastrointestinal system
   - Anorexia
   - Hepatosplenomegaly occurs in long standing cases due to extramedullary haemopoiesis
4. Renal system—concentrating ability of kidneys isdecreased

Other clinical features which may point towards the causative condition leading to anaemia are given in Table 13.6.

COMPLICATIONS

- Angina
- CCF
- Delayed wound healing
- Menstrual disturbances—menorrhagia followed by amenorrhea in severe anaemia
- Loss of libido—in adolescents and adults

IRON DEFICIENCY ANAEMIA

Iron deficiency anaemia is a common cause of anaemia in children. It occurs when there is severe decrease in total body iron content. Classification of iron deficiency anaemia is given in Table 13.7.

TABLE 13.7 Classification of Iron Deficiency Anaemia

Classification	Haemoglobin Level (g/dL)
Mild	10
Moderate	6–10
Severe	< 6

PREDISPOSING FACTORS

- Poor intake of dietary iron (exclusive milk diet, restriction of calories)
- Poor absorption (celiac disease, giardiasis, drug intake)
- Poor bioavailability of iron (breast-milk iron is more bioavailable as compared to that in cow's milk)
- Increased iron requirements (prematurity, twins, ages 3 months to 2 years and 11–16 years, menstruating women, pregnancy and lactation)
- Excess loss of iron (blood loss during child birth, gastrointestinal haemorrhage, faecal blood loss due to hookworm infestation, genitourinary bleed)

Antenatal Period

The placenta is a rich source of transferrin receptor that avidly binds and transfers iron from the mother to the foetus. The majority of iron is transferred during the last trimester of gestation. In the foetus and newborn, iron is stored mainly in the liver and bone marrow. However, the amount of iron stored depends on the length of the gestational period and the weight of the baby at birth. Hence, a preterm or low weight baby is prone for iron deficiency.

Neonatal Period

The timing of the clamping of the umbilical cord at delivery is also a factor in the development of anaemia. The amount of blood transferred to the infant depends on whether the cord is clamped early (less than a minute), intermediately (1–3 minutes) or late (after pulsations cease). For example, if the cord is not cut until pulsations cease, the infants will receive a 20–30 mL/kg body weight transfusion, which is equivalent to approximately 30–35 mg of additional iron.

Infancy

Feeding Pattern

Over the first few months of life, human milk supplies a minimal amount of iron, so stores in the liver and bone marrow are used to meet the iron requirements of the infant. Human milk contains very little iron (about 0.3 mg/L), thus iron stores in the exclusively breastfed infant are depleted quickly so that by 6 months of age most stored iron is used up. If human milk remains the only food source, iron deficiency anaemia develops ultimately. But from 4 to 12 months after the birth, the infant's blood volume doubles. Thus, at this age, dietary sources of iron become critical in order to keep up with this rapid rate of RBC synthesis.

Infections

Parasitic infections, common childhood infectious diseases and malaria predispose infants to blood loss in the stool, depressed erythropoiesis and erythrocyte haemolysis.

CLINICAL FEATURES

Symptoms

- Irritability
- Anorexia
- Easy fatiguability
- Tiredness/weakness
- Leg cramps
- Exertional dyspnoea
- Palpitations
- Inability to concentrate, somnolence, giddiness
- Features of the causative condition, for example epigastric pain (peptic ulcer)
- Constipation
- Pica
- Delayed mental and motor development—even moderate anaemia (Hb <10 g/dL) is associated with depressed mental and motor development in children that may not be reversible. Impaired range of mental and physical functions in children including physical coordination and capacity, mental development, cognitive abilities and social and emotional development is present

Signs

- Eyes—pallor in conjunctiva
- Nails—pallor, koilonychia (spoon-shaped nails), platynychia (flat nails)

- Hair—dry, lustreless hair, excess loss of scalp hair
- Mouth—bald, smooth tongue, glossitis, angular stomatitis
- Abdomen—mild hepatosplenomegaly is common in children

COMPLICATIONS

Other health consequences include reduced immunity and increased morbidity. CCF and angina may manifest in severe persistent cases of iron deficiency anaemia.

D/D OF MICROCYTIC HYPOCHROMIC ANAEMIA

- Iron deficiency anaemia
- Thalassaemia
- Pyridoxine deficiency
- Lead poisoning
- Chronic infections
- Sideroblastic anaemia
- Congenital atransferrinaemia
- Copper deficiency

INVESTIGATIONS

1. Complete blood count with blood indices
   - RBC count decreased, WBC count normal
   - Low mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC)
2. Peripheral blood smear—RBCs are microcytic, hypochromic and show anisocytosis, poikilocytosis
3. Normal reticulocyte count
4. Serum iron levels—less than 60 µg/dL
5. Total iron binding capacity (TIBC)—more than 350 µg/dL
6. Transferrin saturation—less than 16% (normal 25%–50%)
7. Serum ferritin low
8. Free erythrocyte protoporphyrins (FEP)—increased
   - Normal—30–40 µg/dL
   - >70 µg/dL indicate iron deficiency anaemia
9. Stainable iron in the marrow—low
10. FEP/Hb ratio increases. Normal ratio is 60:1
11. Iron containing enzymes such as monoamine oxidase, catalase, cytochrome peroxidases will be low
12. Investigations to determine the cause of anaemia
    - Stool examination—stool for occult blood, ova, cyst (hookworms)
    - Gastrointestinal studies for bleeding, polyp, etc.—Barium meal examination, upper/lower GI endoscopy, etc.

TREATMENT

The treatment of iron deficiency anaemia involves correction of anaemia with haematinics and treatment of the cause of deficiency (e.g., ankylostomiasis, peptic ulcer, bleeding lesions).

Oral Iron Therapy

Elemental iron—1.0–2 mg/kg is given thrice daily for 3–6 months after Hb and other blood values have returned to normal. Oral iron preparations and their iron content are given in Table 13.8. Factors affecting oral iron absorption are given in Box 13.1. Gastrointestinal intolerance is a major side effect.

TABLE 13.8 Iron Preparations for Oral Therapy with the Amount of Iron Content

Oral Iron Preparations	Amount of Iron Content (%)
Ferrous sulphate	20
Ferrous fumarate	33
Ferrous succinate	23
Ferrous carbonate	16
Ferrous lactate	19
Ferrous gluconate	12
Colloidal iron	50

BOX 13.1 Factors affecting oral iron absorption

1. Factors enhancing absorption of oral iron
   - Vitamin C
   - Ferrous salts are better absorbed. Iron has to be converted into ferrous form before it is absorbed. Hence, ferrous salts are preferred as compared to ferric salts.
   - Iron given at bed time is better absorbed as decreased motility of gut during sleep will increase the absorption.
2. Factors inhibiting absorption of oral iron
   - Phosphates in milk
   - Phytates in cereals
   - Ferric salts
   - Oxalates

Response to Oral Iron Therapy

A positive haematological response to treatment is defined as a rise of Hb 0.1 g/dL daily. Sequential response to iron therapy is given in Table 13.9. Failure to respond to oral iron therapy is seen in the following conditions:

- Inadequate iron dose
- Poor patient compliance
- Persistent blood loss
- Impaired intestinal absorption
- Interaction with food and medications
- Associated infections/infestations

Parenteral Iron Therapy

Parenteral Iron Requirement

Calculation of iron requirement is done by using the following formula:

$$\text{Iron requirement (mg)} = \text{Weight (kg)} \times \text{Hb deficit (g/dL)} \times 4.4$$

TABLE 13.9 Response to Iron Therapy

Days	Response to Iron Therapy
12–24 hours	Decreased irritability, improvement in appetite
36–48 hours	Bone marrow response—erythroid hyperplasia
48–72 hours	Reticulocytosis
4–30 days	Hb level increases
3 months	Repletion of iron stores

This formula includes iron needed for replenishment of iron stores.

Preparations

- Iron dextran
- Ferric gluconate (used for dialysis patients)

Indications

- Intolerance to oral iron
- Persistent vomiting or diarrhoea
- Severe bleeding
- Severe gastrointestinal bleeding or lesions where oral iron is contraindicated
- Poor compliance
- Malabsorption syndromes

Intramuscular Iron Therapy

Iron dextran is given as deep intramuscular injection. The child may develop reaction to parenteral iron. Test dose should always be given before giving iron intramuscularly. The injection should be given by 'Z technique' to prevent extravasation of iron into the skin. The skin is pinched and stretched and then the needle is inserted in the skin layer. Now the skin should be pushed to one side before inserting the needle into the muscles. After injecting the drug the skin should be released so that the site of entry in the skin and the muscle are at different sites. This prevents extravasation of iron into the skin.

Intravenous Iron Therapy

Iron dextran carries risk for anaphylaxis. This risk is less for ferric gluconate. Hence, it may be preferred for intravenous use. The dose for intravenous iron is calculated by the following formula:

$$\text{Iron dose required (mg)} = 2.3 \times \text{Body weight (kg)} \times (15 - \text{observed Hb in g/dL}) + \text{500–1000 mg for replenishing iron stores}$$

Red Cell Transfusion

Packed cells can be given very slowly in a dose of 3–5 mL/kg at a time. Diuretics such as furosemide should be given in a dose of 1–2 mg/kg intravenously to prevent volume overload. Indications are as follows:

- Severe anaemia
- Impending CCF due to anaemia

Partial Exchange Transfusion

It is indicated in children with CCF.

PREVENTION

This is a condition which can be prevented easily by supplementing iron-rich feeds. This involves the following measures:

- Eating diet with a wide variety of iron-containing food
- Fortification of articles of food such as bread, salt, wheat and flour
- Improvement of personal hygiene
- Avoiding open air defecation (ankylostomiasis)
- Wearing footwear
- Frequent deworming
- Iron supplementation during pregnancy, lactation and childhood

NATIONAL NUTRITIONAL ANAEMIA CONTROL PROGRAM

It was launched in the country in 1970. It was supposed to cater to children between 1 and 5 years of age. Under this programme, 50% of children were to be given 100 tablets of iron and folic acid (IFA) per year for prophylaxis against nutritional anaemia. However, the children below 24 months cannot swallow the tablets and there is no provision of IFA liquid preparation in the programme. Consequently, the children in this age group largely remained uncovered.

SIDEROBLASTIC ANAEMIA

It comprises of a heterogeneous group of congenital and acquired primary or secondary disorders which have anaemia in common. Congenital sideroblastic anaemia (CSA) is an X-linked recessive disorder, which usually affects male children. It is a rare disorder, which is characterised by mild-to-moderate anaemia with a dimorphic blood picture showing normal red cells and a variable number of microcytes.

PATHOGENESIS

The excess intracellular non-heme iron may result from a diversion of iron, which was intended but not utilised for Hb synthesis. Alternately, excess amounts of iron may be absorbed by the cell because of a failure of normal regulation of iron transfer into the cell. With either event, the excess non-heme iron deposited in the cell may act as a toxin, which either initiates or aggravates intracellular organelle damage finally resulting in ineffective erythropoiesis.

CLINICAL PRESENTATION

The child presents with anaemia. Within this category, the severity of anaemia and the age of presentation vary.

INVESTIGATIONS

- Peripheral smear—normal red cells and a variable number of microcytes.
- Bone marrow studies—ineffective erythropoiesis and the presence of large numbers of ring sideroblasts in the marrow. In the bone marrow, ring sideroblasts are present as a sign of disturbed iron metabolism at a mitochondrial level.
- Iron studies—increased levels of tissue iron and varying proportions of hypochromic erythrocytes in the blood are associated features.

TREATMENT

This condition is generally refractory to therapy. The response to pyridoxine therapy is variable.

MEGALOBLASTIC ANAEMIA

Megaloblastic anaemia refers to anaemia which is characterised by large RBCs with nuclear dysmaturity

(nucleus appears immature relative to cytoplasm) due to impaired DNA synthesis. The most common causes are vitamin B_{12} and folic acid deficiency. Rare metabolic causes include inherited disorders of pyrimidine synthesis (hereditary orotic aciduria), inherited disorders of DNA synthesis, Lesch–Nyhan syndrome, etc. Megaloblastic changes are seen in both haematopoietic and non-haemopoietic cell lines. Anaemia, leucopenia, thrombocytopenia may all be present to variable extents.

PATHOGENESIS

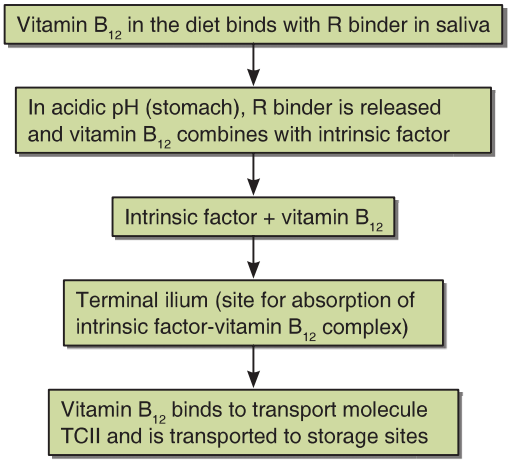
Vitamin B_{12} and folate are coenzymes for the DNA synthesis. Deficiency of either one of these results in the following:

- Impaired DNA synthesis resulting in ineffective erythropoiesis and production of abnormal RBCs. The synthesis of RNA and proteins will be normal.
- Delay in nuclear maturation relative to cytoplasmic maturation. This is known as nuclear–cytoplasmic asynchrony.
- The chromatin clumping is delayed or fails to occur as the normoblast develops from pronormoblast. Nuclear–cytoplasmic asynchrony is also seen in granulocyte precursors resulting in giant metamyelocytes and band forms.
- Megakarycocytes are also large.
- Increase in marrow cellularity. The erythroid myeloid ratio becomes 1:1 (normal is 1:3).
- Nuclear–cytoplasmic asynchrony will be seen in all cells growing rapidly such as mucoid epithelium of the gastrointestinal tract and uterine cervical cells.

Vitamin B_{12} Deficiency

Metabolism of Vitamin B_{12}

Vitamin B_{12} cannot be produced in the human body and should be obtained from the diet. The vitamin B_{12} obtained from diet is bound to the intrinsic factor which is produced by the parietal cells of the gastric mucosa. Vitamin B_{12} is stored in liver. Abnormalities in any of the following steps in vitamin B_{12} transport can lead to its deficiency.



Causes of Deficiency

1. Decreased intake—strict vegetarians and breast-fed infants of strict vegetarian mothers are at high risk of developing vitamin B_{12} deficiency
2. Impaired absorption
   - Achlorhydria
   - Decreased intrinsic factor (pernicious anaemia, after gastrectomy or gastric bypass especially Roux-en-Y bypass)
   - Malabsorption disorders
   - Diverticulosis, fistula, intestinal anastomosis
   - Biological competitions—infection by the fish tapeworm (Diphyllobothrium latum)
   - Selective B_{12} malabsorption (congenital or drug induced)
   - Chronic pancreatitis
   - Ileal resection or bypass
   - Diffuse intestinal disease
3. Increased requirements—hyperthyroidism, pregnancy
4. Impaired utilisation—congenital enzyme deficiencies, lack of TCII

Clinical Features and Investigations

1. Haematological manifestations
   - Anaemia (macrocytic, megaloblastic)—anorexia, irritability, easy fatigability
   - Thrombocytopenia and neutropenia in advanced cases
2. Neurological manifestations

- Peripheral neuropathy (paraesthesia)—pins and needles sensation in the fingers and toes or numbness
- Neurological signs—earliest signs are loss of position and vibration sense
- Subacute combined degeneration of spinal cord—distal sensory loss, absent ankle reflex, exaggerated knee jerk, extensor plantar
- Irritability, convulsions, retrobulbar neuropathy and mental retardation

3. Psychiatric manifestations
   - Personality or memory changes
   - Depression, irritability, psychosis and dementia
4. Miscellaneous
   - Hyperpigmentation over the back of the hands, fingers and nose
   - Glossitis and stomatitis
   - Other features—hepatosplenomegaly, signs of malabsorption, abdominal scar due to ileal resection, etc.

Investigations are given in Box 13.2.

Complications

Subacute combined degeneration of the spinal cord occurs due to demyelination secondary to deficiency of vitamin B_{12}. This results in impairment or loss of proprioception.

Treatment

- Vitamin B_{12}—100 µg of cyanocobalamin or hydroxycobalamin is given three times a week intramuscularly till the Hb is normal. Following this, the child is given 100 µg intramuscularly weekly and then monthly. Reticulocytosis occurs within a week after starting the treatment.
- When associated with neurological complications, the dose can be increased to 500–1000 µg.
- In children with transcobalamin II deficiency or with neurological manifestations, high doses of vitamin B_{12} should be given intramuscularly. Initially 100–1000 µg should be given everyday for 1–2 weeks followed by same dose once in every 1–3 months. Such high doses are given as the absorption is variable in doses below 500 µg or less.
- Once haematological remission is seen, intranasal vitamin B_{12} in a metered dose of 500 µg once weekly can be given.

Follow-up

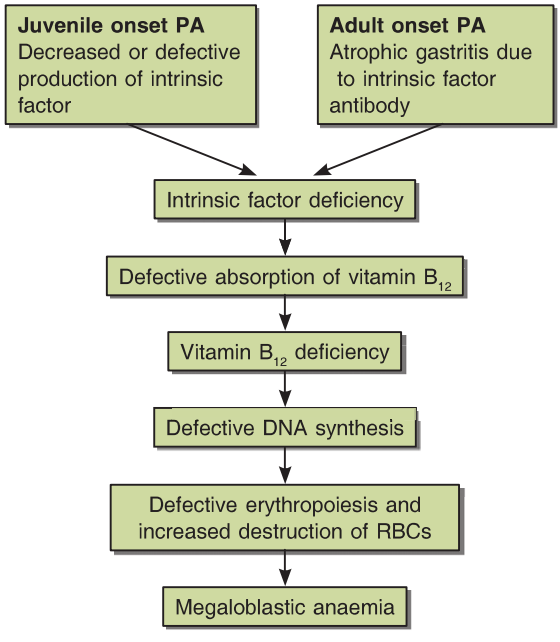
Serum vitamin B_{12}, homocysteine, methymalonic acid levels in the blood should be checked.

Pernicious Anaemia

It is also known as Biermer's anaemia, Addison's anaemia or Addison–Biermer's anaemia. This condition was first described by Thomas Addison in 1849. It is a form of megaloblastic anaemia that is characterised by impaired absorption of vitamin B_{12} due to lack of intrinsic factor. It occurs as a result of loss of parietal cells in the stomach (usually as a result of atrophic gastritis).

Pathophysiology

In autoimmune atrophic gastritis, autoantibodies are directed either against the parietal cells of the stomach or against the intrinsic factor, so that the binding of vitamin B_{12} with intrinsic factor is impaired.



Pathological Changes. The following pathological changes are seen:

- Alimentary tract—atrophic gastritis of autoimmune origin is more common in adults with pernicious anaemia. Autoimmune destruction of gastric parietal cells leads to lack of intrinsic factor which predisposes to vitamin B_{12} deficiency.
- Central nervous system—myelin degeneration of dorsal and lateral tracts in the spinal cord results in subacute combined degeneration.
- Bone marrow—hypercellular marrow.

Clinical Features

A child with pernicious anaemia usually presents with following features:

- Sore tongue—atrophic glossitis (shiny, glazy, beefy red)
- Paraesthesia
- Weakness (peripheral neuritis)
- Weakness, clumsiness, unsteady gait (due to spinal cord involvement)

Investigations

- Complete blood count—anaemia
- Blood smear study—megaloblasts
- Pentagastrin or histamine gastric analysis
- Serum parietal cell and intrinsic factor antibodies
- Serum vitamin B_{12} levels
- Blood levels of methylmalonic acid or homocysteine

Treatment

Lifelong vitamin B_{12} replacement is required. Vitamin B_{12} injections can be given. Oral vitamin B_{12} supplements are given in large doses (1–2 mg/day) at about 200 times more than the normal daily requirement. Nasal and sublingual vitamin B_{12} are under trial.

Complications

In a child with pernicious anaemia the following complications can occur:

- Risk of gastric cancer is 2–3 times greater than the normal people of same age
- Carcinoids are more common in patients with pernicious anaemia
- Permanent neurological damage

Prognosis

Neurological complications can be permanent if not treated early. Death can occur.

Folate Deficiency

Causes

- Decreased intake—inadequate diet, goat's milk consumption
- Increased needs—infancy, pregnancy, hyperthyroidism, chronic haemolytic disease
- Impaired absorption—malabsorption disorders, intestinal or jejunal resection
- Impaired utilisation due to use of drugs such as dihydrofolate reductase inhibitors (methotrexate, trimethoprim, triamterene, pyrimethamine), purine synthesis antagonists (6-mercaptopurine), pyrimidine antagonists (cytosine arabinoside), phenytoin and oral contraceptives
- Increased losses (haemodialysis)

Combined deficiency of vitamin B_{12} and folate is seen in tropical sprue.

Clinical Features and Investigations

- Anorexia, weakness, irritability
- Anaemia
- Chronic diarrhoea
- Ulcers
- Glossitis (painful tongue)
- Impaired immunity
- Haemorrhage due to thrombocytopenia
- Increased homocysteine predisposing to atherosclerosis

BOX 13.2 Investigations in megaloblastic anaemia

1. Complete Blood count
   - Haemoglobin decreased
   - RBC count decreased
   - Platelet count may be decreased
   - MCV >100 fL (normal 82–92)
   - MCH increased
   - MCHC normal
   - Reticulocyte count decreased due to increased destruction of fragile and abnormal megaloblastic erythroid precursors
   - Large number of megaloblasts is seen in peripheral smear. These are immature and dysfunctional RBCs
   - Neutrophils are large and hypersegmented

2. Morphological changes in RBCs
   - Central pallor—absent
   - Anisocytosis—variation in size of RBCs
   - Poikilocytosis—variation in shape of RBCs
   - Macrocytes—large RBCs
   - Macro-ovalocytes—oval-shaped large RBCs
   - Nucleated red blood cells may be seen in the smear
   - Howell–Jolly bodies (chromosomal remnants from the RBCs)
3. Biochemical analysis
   - Serum and red blood cell folate levels are low in folate deficiency
   - Serum vitamin B_{12} assay
   - Increased lactate dehydrogenase (LDH) levels especially isoenzyme LDH-2, as a marker of ineffective erythropoiesis
   - Increased homocysteine and methylmalonic acid levels in blood and urine in vitamin B_{12} deficiency. (Normal methylmalonic acid levels will rule out vitamin B_{12} deficiency. Methylmalonic acid will be elevated in vitamin B_{12} deficiency. Vitamin B_{12} is one of the prosthetic group of the enzyme methylmalonyl-coenzyme A mutase. Deficiency of vitamin B_{12} results in defective metabolism of methylmalonic acid which results in accumulation in blood and urine.)
   - Increased homocysteine in folic acid deficiency
4. Bone marrow study
   - Hypercellular marrow with megaloblastic changes in all stages of red cell development
   - Pronormoblast will be large and will have normal fine chromatin pattern
   - Normoblast will not have chromatin clumping
5. Schilling test (see Chapter 4)
6. Formiminoglutamic acid (FIGLU) excretion test
7. Jejunal biopsy may show villus atrophy

Folic acid deficiency in the pregnant mothers predisposes to neural tube defects (spinal dysraphism, meningomyelocele) in the babies.

Investigations are given in Box 13.2.

Treatment

Folic acid should be given in doses of 0.5–1.0 mg/day for 3–4 weeks in established cases. Doses of folate more than 0.1 mg can correct anaemia due to vitamin B_{12} deficiency but will precipitate the neurological manifestations. In conditions with coexisting deficiency of vitamin B_{12}, vitamin B_{12} must be given before folate.

DIFFERENTIAL DIAGNOSIS

All cases of macrocytic anaemia may be confused with megaloblastic anaemia. Some of these include:

- Aplastic anaemia
- Early iron deficiency anaemia
- Hypothyroidism

HAEMOLYTIC ANAEMIA

It occurs due to increased destruction or shortened lifespan of erythrocytes.

The normal lifespan of RBCs is about 120 days. When excessive destruction of RBCs occurs, the bone marrow can compensate by increasing the red cell production by about 7–8 times. Haemolytic anaemia results when the production cannot compensate for the destruction.

Causes of haemolytic anaemia are as follows (see section *Hemolysis*, page 663):

- Defects of Hb
- Defects of red cell membrane
- Defects in red cell metabolism
- Antibody—mediated
- Mechanical injury/thermal injury
- Infection induced
- Drugs/ toxins/chemicals/poisons (Box 13.3)
- Renal/liver disease/malignancy

Evidence of increased haemolysis:

- Increased reticulocyte count (increased red cell production in the marrow)
- Jaundice (due to increased haemolysis)
- Anaemia (due to increased haemolysis)
- Hypercellular marrow—(increased bone marrow activity)
- Haemoglobinaemia

BOX 13.3 Drugs causing haemolytic anaemia

1. Chemicals
   - Naphthalene
   - Aniline dyes
2. Drugs
   - Antibiotics—chloramphenicol, nalidixic acid, penicillin
   - Antimalarials—primaquine, quinine, quinacrine
   - Analgesics—acetyl salicylic acid
   - Vitamin K analogues
   - Methyldopa
3. Poisons
   - Phenylhydrazine
   - Trinitrotoluene
   - Benzene, nitrobenzene
   - Methyl chloride
   - Arsenic
   - Lead
   - Snake venom

- Haemoglobinuria
- Decreased serum haptoglobin and haemosiderinuria

THALASSAEMIA

It is an autosomal recessive haemolytic anaemia that results from defective production of Hb due to mutation in the genes which direct the production of Hb (a protein that carries oxygen to the cells and tissues of the body).

Beta-thalassaemia is the most common single-gene disorder. Patients with thalassaemia produce abnormal Hb that cannot transport enough oxygen to tissues. This produces symptoms ranging from fatigue to organ damage.

Aetiology

Haemoglobin is made up of four chains of amino acids: two identical α-chains and two identical β-chains. Many different mutations in the gene coding for these chains cause thalassaemia, but all the mutations can be divided into two main groups. Some mutations affect the structure of α- or β-chains, while others affect the rate at which the chains are produced. In general, mutations that affect the structure of the chains result in more severe disease than mutations that affect the rate at which the chains are produced.

Genetics

Two copies of the abnormal, recessive gene are required for the disease to occur. A person who has just one copy of the mutated gene is termed a carrier, since he or she carries the gene but is not affected by it.

When two carriers of β-thalassaemia have children, each child has a 25% chance of inheriting two abnormal copies of the β-gene and, therefore, developing the disease. Each child has a 50% chance of inheriting one abnormal gene and being a carrier, and a 25% chance of inheriting two normal β-genes (Fig. 13.4).

The inheritance of α-thalassaemia is more complicated because each person normally has four copies of the α-gene, two inherited from each parent. People with one or two abnormal α-genes are carriers and do not develop the disease. Children who inherit three abnormal α-genes have a form of α-thalassaemia that makes them anaemic but typically does not shorten their lifespan. Those who inherit four abnormal α-genes have a severe form of α-thalassaemia that results in death in the womb or within the first few hours of life.

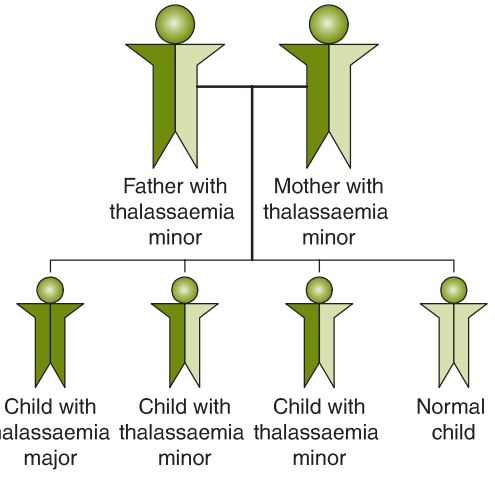


FIGURE 13.4 Thalassaemia pedigree.

Carriers

They typically do not have symptoms of thalassaemia and do not require treatment. In fact, carriers of thalassaemia are partially resistant to malaria, a serious and often fatal parasitic disease. In some areas where malaria is common, up to 20% of people are thalassaemia carriers. Some believe that the thalassaemia genes have become widespread in these areas because of the advantage these genes confer on carriers.

Pathogenesis

An imbalance in α- and β-chain production has several consequences for RBCs. The amount of normal Hb in a thalassaemia patient's red cells is reduced, so less oxygen is carried to the tissues. In addition, the chain that is produced in normal quantities forms insoluble clumps inside red cells. These clumps damage the cells, which are rapidly removed from the bloodstream, resulting in anaemia.

The body in an attempt to correct the anaemia, increases the production of RBCs in the bone marrow. But these new red cells are destroyed almost as quickly as they are produced because they too are abnormal.

The synthesis of γ-chain continues after birth. Hence, the HbF which has more affinity to oxygen is increased. This results in tissue hypoxia. This will stimulate production of more erythropoietin. This results in increased medullary and extramedullary erythropoiesis.

Eventually, the bone marrow expands, causing bones to become thin and weak, and the child suffers repeated fractures. The expansion of the marrow also changes the shape of the bones, stunting the child's growth and distorting the shape of the head and face. The liver and spleen become greatly enlarged because red cell production also occurs in these organs.

Types

1. Beta thalassaemia—a mutation in the β-genes decreases the production of β-chains, resulting in β-thalassaemia.
2. Alpha thalassaemia—a mutation in the α-genes decreases the production of α-chains, resulting in α-thalassaemia.

Beta Thalassaemia

Beta thalassaemia is generally much more severe than α-thalassaemia. Untreated, it is usually fatal in the first few years of life.

Clinical Variants

Depending upon the clinical severity, the following variants of β-thalassaemia are recognised:

- Thalassaemia major, which is the commonest type (Table 13.10)
- Thalassaemia intermedia
- Thalassaemia minor

These variants are designated as follows:

- β—normal β-globin chains

TABLE 13.10 Clinical Variants of Thalassaemia

Features	Thalassaemia Major ($\beta^0\beta^0$)	Thalassaemia Intermedia ($\beta^+\beta^+$ or $\beta^0\beta^+$)	Thalassaemia Minor β^0 or β^+
Genetics	Homozygous form—two mutated genes	Homozygous or heterozygous form; two mutated genes	Heterozygous form—one normal and one mutated gene
Age of presentation	Early infancy (6–18 months)	Presents by second year of life	Adolescence
Clinical features	Progressive pallor Hepatosplenomegaly Bony changes	Anaemia Hepatsplenoomegaly Bony changes	Mild persistent anaemia
Requirement of blood transfusion	By the age of 6 months	Rarely needed. By 2 years Hb level may fall to about 7 g/dL	By adolescence
Complications	Hypersplenism Iron overload	Iron overload Cholelithiasis	Iron overload
Prognosis	Fatal in first few years of life	Normal lifespan	Normal lifespan

- β^0—no formation of β-chains
- β^+—demonstrable β-chain production

Thalassaemia Major ($\beta^0\beta^0$). It is also known as Cooley's anaemia and is the most severe form of β-thalassaemia. It is characterised by a transfusion-dependent anaemia, growth retardation, massive splenomegaly, jaundice and characteristic haemolytic facies. The death may occur in the first few years due to severe anaemia, cardiac or liver failure. Also iron overload can lead to haemosiderosis, which leads to complications and death in second decade of life.

Thalassaemia Intermedia ($\beta^+\beta^+$ or $\beta^0\beta^+$). The clinical manifestations are in between thalassaemia major and minor. It presents with anaemia of intermediate severity (Hb ≥8 g/dL), usually at the age of 2 years. It does not require regular blood transfusions. The patients lead a near-normal life. The diagnosis is made at the age of 4–5 years. The children have mild hepatosplenomegaly. Haemoglobin electrophoresis reveals HbF (10%–50%), HbA_2 (>4%) and HbA (about 30%).

Thalassaemia Minor $\beta^0(\beta\beta^0)$ or $\beta^+(\beta\beta^+)$. It is also known as thalassaemia trait or thalassaemia carrier. This is the mildest form of the illness. These patients have mild anaemia, abnormal red cell indices (MCV and MCH reduced, normal MCHC), and abnormal Hb electrophoresis. Level of HbA_2 estimation (≥3.5%) is the gold standard for the diagnosis of thalassaemia trait.

Beta Thalassaemia Associated with β-Chain Structural Variants. The most significant condition in this group of thalassaemic syndromes is the Hb E/β thalassaemia. It may present with severity similar to thalassaemia intermedia or thalassaemia major.

Clinical Features

An infant born with β-thalassaemia initially appears normal. As the HbF comes down at 3–6 months of age, the symptoms of thalassaemia manifest with increasing pallor. Children remain asymptomatic up to 6–8 months of age in most cases. It should be suspected in any child who presents with microcytic, hypochromic anaemia and does not respond to treatment with iron. Clinical features include the following:

- Anaemia—irritability and fatigue
- Fever and diarrhoea (repeated infections)
- Failure to thrive
- Jaundice
- Haemolytic facies—maxillary hyperplasia, prominent parietal eminence, frontal and occipital bossing (big squarish head), prominent malar bones, widely spaced eyes, depressed nasal bridge (Fig. 13.5; also see Table 3.9). The unequal development of the upper and lower jaws leads to malocclusion of teeth so that the upper teeth are projected forwards
- Hepatosplenomegaly
- Delayed sexual development

Investigations

Before 6 months of age

- DNA-based diagnostic studies
- Rate of globin chain synthesis
- Naked eye single tube red cell osmotic fragility test (NESTROFT)

After 6 months of age

- Haemoglobin low (3–9 g/dL), total RBC count and haematocrit decreased.
- Peripheral smear—RBCs normal/microcytic, hypochromic anaemia with anisocytosis and poikilocytosis. Target cells and tear drop cells will be seen. There will be marked basophilic stippling and variable polychromasia. Fragmented red cells, nuclear remnants such as Howell–Jolly



FIGURE 13.5 Haemolytic facies in a thalassaemic child who has undergone splenectomy. Note the splenectomy scar.

bodies and Heinz bodies may be seen. A large number of early, intermediate and late erythroblast will be seen.

- Red cell indices—MCV/MCH/MCHC may be normal or low.
- Mild leucocytosis and thrombocytosis may be present due to the stimulation of the bone marrow. Leucocytosis with shift to left is seen during acute haemolytic episodes.
- Reticulocyte count will be increased due to increased production of the RBCs to compensate for the haemolysis.
- Haemoglobin electrophoresis and high-performance liquid chromatography (HPLC)—HbA_2 raised, HbF may be raised. Different types of Hb in a patient's blood are measured to distinguish between normal individuals, carriers and people with thalassaemia. This test should be done before blood transfusion is given, as the formation of the HbF is suppressed by blood transfusion. Using the electrophoresis method to test a child's parents and establish that they are both carriers helps confirm the diagnosis.
- Bone marrow is hypercellular with erythroid hyperplasia. There is increased number of stippled erythroblasts and sideroblasts. During the aplastic crisis, the marrow cellularity is decreased.
- Screening for genetic counselling.
- Osmotic fragility test shows increased resistance to haemolysis even in the presence of anaemia. The cells in these patients are thinner and absorb more water.
- Urinary urobilinogen—markedly increased.
- Stool examination—stools are dark in colour due to increased stercobilinogen. Normal excretion of stercobilinogen is 40–180 mg in 24 hours. This may exceed to 200 mg.
- Serum iron—increased.
- Serum bilirubin level—moderately elevated. This depends upon the rate of haemolytic activity, functional capacity of the liver to excrete bilirubin and the mass of Hb available for haemolysis.
- Radiological changes—medullary portion of the bone is widened and the bony cortex is thinned out with a coarse trabecular pattern in the medulla. X-ray of the metacarpals, ribs and vertebra shows thinning of cortex. X-ray of the skull shows hair on end appearance. This is due to widened diploic spaces in the skull. The frontal bone appears thickened, starting in the nasal region of the frontal bone and extending symmetrically over the parietotemporal regions but sparing the occiput. This gives the appearance of bossing. Pneumatisation of the sinuses is delayed and the maxilla appears overgrown with prominent malar eminencies. X-ray of bone changes is seen after 1 year. X-ray of hand shows reticular pattern in metacarpals (after 4 months); chest shows reticular pattern in ribs.
- Coagulation studies may be abnormal.
- Investigation for complications—glucose tolerance test, endocrine studies and serum calcium.

Management

It consists of a step-wise approach which includes the following:

1. Confirmation of diagnosis
2. Correction of anaemia
3. Prevention/treatment of iron overload by chelating agents
4. Pharmacological methods
5. Curative treatment—bone marrow transplantation and stem cell therapy
6. Genetic counselling
7. Treatment of complications

Confirmation of Diagnosis. It is done by clinical evaluation and investigations as discussed above.

Correction of Anaemia by Blood Transfusion. Patients with β-thalassaemia major require regular blood transfusions. These alleviate the symptoms of anaemia and suppress the production of patient's own defective red cells, allowing bone marrow to return to normal size and bones to return to their normal shape.

Regimens. Different regimens are used depending on the target Hb levels (Table 13.11). Hypertransfusion regime is preferred as it permits normal growth, prevents anaemia and its complications, suppresses erythropoiesis, prevents skeletal changes, prevents gastrointestinal iron absorption, inhibits extramedullary haemopoiesis, thus preventing splenomegaly and hypersplenism. Disadvantage of hypertransfusion regime is that it needs more blood at the start of therapy. Pre-

TABLE 13.11 Transfusion Regimens in Thalassaemia

Transfusion Regimen	Maintenance Hb level (g/dL)
Low transfusion	6–10
Hypertransfusion	10–12
Super transfusion	12–14

transfusion levels should be maintained at 10 g/dL or more to inhibit marrow activity. Post-transfusion levels should not be more than 16 g/dL to avoid the complications associated with hyperviscosity.

Leucocyte Filters. The leucocytes in the transfused blood give rise to non-haemolytic febrile transfusion reactions. These are prevented by the use of leucocyte filters. Use of chlorpheneramine maleate and paracetamol may give relief.

Component Therapy. Packed RBC transfusion and neocyte transfusion may be done. The neocytes have a longer lifespan. The infusion of the neocytes will lead to the increase in the interval between two transfusions. This also decreases the risk for iron overload.

Amount and Rate of Transfusion. A total of 20 mL/kg of fresh blood is transfused every 2–4 weeks. If packed cells are used, 10 mL/kg is given.

The blood should be transfused at a rate of 5–7 mL/kg/hour. In presence of cardiac failure, the rate of transfusion should be decreased. The Hb should increase by 3.5 g/dL.

Average annual blood requirement is 180–200 mL/kg. In patients with hypersplenism or antired cell antibodies, the requirement is more.

Iron Overload and Chelation Therapy. Iron overload is due to repeated transfusions and increased iron absorption from the gastrointestinal system. The transfusion regimens interrupt the body's normal recycling of iron. The body is unable to excrete iron, and with each transfusion of red cells, iron gradually accumulates in the body, with damaging results. If untreated, the toxic build up of iron leads to death usually from heart failure in a patient's late teens. Unchelated blood transfusion predisposes to endocrinopathies such as hypoparathyroidism, which results in hypocalcaemia, hypereflexia, seizures and tetany.

To prevent the fatal accumulation of iron, patients are treated with iron chelating agents which bind iron and allow it to be excreted from the body. The most widely used iron chelator is desferrioxamine.

Chelating Agents. These are indicated when serum ferritin levels are more than 1000 µg/L. The aim is to keep the serum ferritin levels below 1000 µg/L. Following are the drugs used:

1. *Desferrioxamine (DFO)* is given subcutaneously as continuous infusion over a period of 8–12 hours/day for 5–6 times/week. One gram of DFO binds 85 mg of iron. Microinfusion pumps can be used to infuse this drug. It is delivered through a needle placed under the skin and attached to a small pump. Many patients find this intensive treatment regimen difficult to maintain, and some do not wear the pump long enough to eliminate all of the excess iron from their body (Fig. 13.6). The daily dose is about 30–70 mg/kg according to the serum ferritin levels (Table 13.12). The total dose should not exceed 100 mg/kg/day. Addition of vitamin C,100 mg daily, prior to DFO therapy helps in



FIGURE 13.6 Urine examination in a case of thalassaemia after treatment with desferrioxamime. Urine is dark in colour due to excretion of iron. Compare with the control which is normal in colour.

TABLE 13.12 Dose of Desferrioxamine

Serum Ferritin Level (µg/L)	Dose of DFO (mg/kg/day)
<2000	25–50
2000–3000	35
>3000	55

conversion of haemosiderin (insoluble form) into ferritin (soluble form). Iron can be chelated from ferritin. Adverse effects of DFO are as follows:

- Thinning of retinal vessels (defect in visual field, dark adaptation)
- Sensorineural hearing loss
- Metaphyseal dysplasia

2. *Deferriprone (Kelfer)* is an oral iron-chelating agent given in a dose of 75–100 mg/kg/day in two to three divided doses. Adverse effects are as follows:
   - Arthropathy
   - Agranulocytosis
   - Drug induced lupus
   - Idiosyncratic reaction (neutropenia, thrombocytopenia)
   - Increased liver enzymes
   - Zinc deficiency
3. Combination of DFO + Kelfer for 1–6 days/week. Advantage is that they act at different sites. Vitamin C 100 mg/day helps in excretion of iron

Splenectomy. Splenectomy should be postponed for at least up to the age of 6 years to avoid the risk of infections. Indications are as follows:

- Transfusion requirement of packed cells more than 200 mL/kg/year
- Hypersplenism (leucopenia, thrombocytopenia)
- Reduced RBC survival (Cr51 radioisotope studies)
- Massive splenomegaly

The child should be immunised with pneumococcal vaccine, *Haemophilus influenzae* vaccine and meningococcal vaccine 4–6 weeks prior to splenectomy. Life-long penicillin prophylaxis should be given. Prophylaxis for malaria can also be given.

Increased Synthesis of HbF by Drugs. New treatments to help thalassaemia patients have focussed on HbF. It is made up of two α-chains and two γ-chains. Soon after the birth, the gene that produces the γ-chain is turned off and the gene that produces the β-chain is turned on. Most patients with β-thalassaemia have normal γ-genes and can produce normal HbF. Efforts have been made to decrease the excess of α-chains by increasing the γ-chains. The increased γ-chains combine with the excess of α-chains to form the HbF. The patients with β-thalassaemia who continue to produce HbF after birth have milder disease.

Treatment that would turn a patient's γ-genes back on again is being tried. The resulting increase in HbF in the blood would work just like blood transfusion, relieving the symptoms of anaemia and allowing bones to return to their proper shape, without side effects of blood transfusion.

Drugs that stimulate the production of γ-chains are butyrates, hydroxyurea, 5-azacytidine and erythropoietin.

Butyrates are given in a dose of 200–400 mg/kg/day intravenously slowly over 6–8 hours. This raises the HbF level by 8%–12%.

Bone Marrow Transplantation. Bone marrow from a histocompatible donor should be harvested and transplanted. It offers permanent cure.

Stem Cell Transplantation. Currently the only way to cure thalassaemia is by transplantation of stem cells, the cells in bone marrow that are responsible for blood cell formation. In this procedure, the bone marrow is destroyed with large doses of radiation or chemotherapy; then the patient's defective stem cells are replaced with normal stem cells from an immunologically compatible donor, usually a sibling. Sources of stem cells are cord blood, peripheral blood, bone marrow and foetal liver. Unfortunately, stem cell transplantation can help only a minority of thalassaemia patients. Fewer than 25% of patients have a compatible sibling who could donate stem cells. Further, even if a compatible donor is available, anaemia and other complications of thalassaemia make some patients too sick to undergo transplantation. The transplant procedure itself can result in severe complications or even death.

Antenatal Diagnosis and Genetic Counselling. Prenatal diagnosis is done by foetal DNA analysis by blood sampling around 16–18 weeks of intrauterine life. As it is an autosomal recessive disorder, genetic counselling is always helpful for the prevention of disease.

Recent Advances

- Scientists have developed technologies to pinpoint which of the hundreds of known thalassaemia mutations an individual patient has. This may allow doctors to predict the severity of the patient's disease.
- Gene replacement therapy—efforts are made to correct the genetic defect by transferring the normal genes into the stem cells. This is still in experimental stage.

Monitoring. It is done for the following:

- Annual blood requirement (average 180–200 mL/kg)
- Growth monitoring—growth and development
- Antibodies against red cells
- Hypersplenism
- Iron overload
- Serum ferritin levels
- Liver function tests
- Cardiac evaluation
- Radiological evaluation—X-ray spine metaphysis
- Endocrinal evaluation—diabetes, hypogonadism

Prognosis

It depends on the severity of the disease.

- If untreated, β-thalassaemia is usually fatal within a few years.
- The lack of oxygen gradually damages various organs in the body, and most patients die in childhood due to severe anaemia, cardiac failure or intercurrent infection.
- Repeated transfusions can lead to various organ failures if the child survives longer.
- Life expectancy for patients with thalassaemia has steadily increased over the last several decades. With transfusion and chelation regimens, 90% of patients survive at least to age 25.

Alpha Thalassaemia

In α-thalassaemia, red cells are not destroyed as rapidly as in β-thalassaemia. Patients with α-thalassaemia usually have mild to moderate anaemia and may develop an enlarged spleen. However, they do not usually suffer from bone abnormalities of growth retardation, and most patients survive to adulthood. In many cases, no treatment is necessary.

Prevention

- Antenatal diagnosis
- Genetic counselling

Antenatal Diagnosis

- Estimation of the rate of globin synthesis in the foetal blood samples—DNA mutation analysis
- Prenatal diagnosis and selective abortion of the affected foetus
- Carrier screening—level of HbA2 ≥3.5%

Genetic Counselling. The most effective approach to reduce the burden of the society and to reduce the disease incidence is implementation of a carrier screening programme, genetic counselling, prenatal diagnosis and selective termination of affected foetuses. Prenatal diagnosis of thalassaemia through procedures such as amniocentesis and chorionic villus sampling is available in many medical centres, and some couples may choose to abort severely affected foetuses. Sensitivity ranges from 94% to 99%.

SICKLE-CELL DISEASE

It is an inherited blood disorder which occurs due to a point mutation in the β-globin gene located on chromosome 11. Thiamine is changed for adenine at the sixth codon of the β-globin gene. This change results in replacement of valine for glutamic acid in the sixth position in the β-polypeptide chain.

The red cells are sickle shaped (hence called sickle-cell anaemia) and do not function normally. This results in premature destruction of RBCs. Geographical distribution of sickle-cell gene is similar to that of malaria-infected areas. This carries a survival value as children with sickle-cell trait are resistant to malarial infection.

Types

1. Sickle-cell trait—heterozygous state(HbAS); only one β-globin gene has sickle-cell mutation.
2. Sickle-cell disease/syndrome—it occurs when one β-globin gene has sickle-cell mutation, while the other β-globin gene also has some mutation, which may be similar to or other than sickle-cell mutation. HbS is >50% of the total Hb. It consists of the following types:

- HbSS or HbS or sickle-cell anaemia—it occurs in patients who are homozygous for HbS gene. Both β-globin genes have sickle-cell mutation. HbS is >90% of the total Hb
- HbSC—sickle–Hb C disease
- HbS/β^0—sickle-β^0-thalassaemia (has similar course such as HbSS)
- HbS/β^+—sickle-β^+-thalassaemia
- S hereditary persistence of foetal haemoglobin (HPFH)

Factors Precipitating Sickling of Cells

Sickling of cells is precipitated by acidosis (local or systemic), exposure to cold, dehydration, exertion or physical stress, fever, hypoxia and infection. It can be demonstrated in peripheral smear by following methods:

- Addition of 2% sodium meta-bisulphate (a reducing agent that deoxygenates blood) to the smear and allowing it to stand for a few hours. The edges of the cover slip should be covered by paraffin to prevent drying.
- Application of tourniquet around the limbs or fingers results in hypoxia and acidosis, thereby causing sickling.

Sickle-Cell Anaemia (HbS or HbSS)

Clinical Features

- Growth retardation
- Delayed milestones
- Anaemia
- Icterus
- The spleen is moderately enlarged in the childhood. Repeated infarction leads to shrinking of spleen and later autosplenectomy
- Delay in development of secondary sexual characters
- Chronic non-healing ulcers in the leg
- Bony deformities such as kyphosis and scoliosis may be seen
- Fever
- Pain—bone pain, abdominal pain and vomiting, painful priapism due to occlusion of blood flow from corpora cavernosa by the sickled cells, chest pain
- Haematuria due to infarction of kidneys
- Polyuria due to loss of concentrating power of kidneys and the involvement of renal vasculature
- Central nervous system—focal neurological defects (monoplegia, hemiplegia), convulsions
- Vaso-occlusive crisis

Complications

1. Sickle-cell crisis/vaso-occlusive crisis is due to sudden and rapid sickling of RBCs in the blood vessels. It may be associated with fever and leucocytosis. The tendency for sickling increases when the blood is deoxygenated. In the capillaries when the blood flow is sluggish, the oxygen is utilised by the tissues and sickling occurs. As the sickle cells are rigid, they predispose to obstruction of the vessels, and lead to ischaemia. This leads to sickle-cell crisis. The crisis lasts for 5–7 days. It most commonly manifests as pain. It may present as dactylitis, hand and foot syndrome, autosplenectomy, renal papillary necrosis, acute chest syndrome, retinal haemorrhages, avascular necrosis of femoral head, painful priapism and stroke
2. Immunological system—functional asplenia usually occurs by the age of 5 years. In few children, it can occur by the age of 6 months due to autosplenectomy. This leads to increased risk of infections by capsulated organisms such as *Streptococcus pneumoniae* and *H. influenzae*. Infection with parvovirus B19 causes red cell aplasia and may lead to aplastic crisis
3. Skeletal system
   - Osteomyelitis due to salmonella or staphylococcus. It should be treated with antibiotics for 4–6 weeks
   - Hand foot syndrome and dactylitis
   - Aseptic necrosis of head of femur
4. Haematological complications
   - Acute splenic sequestration in infants is seen in association with bacteraemia, upper respiratory infections or viral infections. Spleen size enlarges. Haemoglobin decreases by 2 g/dL or more with hypovolaemia
   - Thromboembolic manifestations such as sudden blindness and neurological defects

5. Neurological system
   - Strokes with/without associated focal neurological deficit
   - Cerebral venous thrombosis
   - Reversible posterior leukoencephalopathy syndrome (RPLS)
6. Respiratory system complications
   - Acute chest syndrome—characterised by fever, respiratory distress and chest pain. It is usually associated with infection. New radio-opaque densities on radiograph may be seen due to single lobe, left lower lobe or multiple lobe involvement
   - Unilateral or bilateral pleural effusion
   - Bronchiolitis
   - Asthma
   - Pneumonia
   - Pulmonary hypertension
7. Gentourinary system complications—Sickle-cell nephropathy includes papillary necrosis, isolated haematuria, nephritic syndrome, renal infarcts, pyelonephritis, renal medullary carcinoma
8. Miscellaneous
   - Ulcer in the legs
   - Gall stones
   - Multiple organ failure

Investigations

1. Red Blood count—anaemia.
2. Differential count—leucocytosis with shift to left is seen during acute haemolytic episodes.
3. Haemoglobin level—decreased.
4. Platelet count—usually normal or may be elevated.
5. Peripheral smear study—shows anaemia and sickle cells. Other findings are as follows:
   - Microcytes, anisocytosis, poikilocytosis, polychromasia, punctuate basophilia stomatocytes, target cells and nucleated RBCs are seen.
   - Howell–Jolly bodies are present if the patient has functional asplenia.
   - Reticulocyte count is increased due to increased production of the RBCs to compensate for the haemolysis.
6. Radiological studies
   - X-ray of skull—ground-glass appearance.
   - X-ray of the long bones may show cortical thickening and patchy irregularities.
7. Electrophoresis of the Hb—shows more than 60%–80% of HbS in sickle-cell anaemia.
8. Sickling test.
9. CT scan/MRI/MR venography for cerebral venous thrombosis.
10. Doppler to assess the blood velocity.

Treatment

There is no specific treatment. The aim of the treatment is to control the symptoms and treat the complications. It consists of the following steps:

- Management of pain and anaemia
- Management of sickle-cell crisis
- Management of complications
- Prevention of infections by capsulated organisms

Management of Pain. Treatment of pain consists of the following:

1. Acetaminophen
2. Intravenous morphine or morphine derivatives
3. Hydroxyurea is effective in painful episodes. It is safe in children above 5 years of age. It is given in a dose of 15–20 mg/kg daily. The dose is increased by 2.5–5 mg/kg every 8 weeks until the maximum dose of 35 mg/kg is reached. Advantages of hydroxyurea:
   - Decreases the painful episodes
   - Raises Hb level
   - Raises HbF level
   - Decreases the rate of ACS episodes and blood transfusion

Treatment of Anaemia

- Blood transfusion for haemodynamic stability and to maintain the Hb level at 10–11 g% with blood transfusions. Haematocrit more than 10–11 g% will lead to increased viscosity of the blood, and sluggish blood flow which predisposes to hypoxia and sickle-cell crisis.
- Exchange transfusion may be done to maintain the HbS at <50% or less preferably <30%.
- Drugs that increase the production of HbF in the bone marrow (hydroxyurea).

- Bone marrow transplantation could be of help.
- Folic acid supplement may be needed throughout the life. Folate requirement may be increased due to increased haemopoietic activity.

Treatment of Sickle-Cell Crisis

- Blood transfusion should be avoided at the time of sickle-cell crisis, as this increases the viscosity and decreases the speed of the blood flow. This results in hypoxia and acidosis which further aggravates the sickling of RBCs.
- Transfusion with plasma or plasma volume expanders (dextran) improves the circulation by reducing the haematocrit and thereby reducing the viscosity of the blood.
- Acidosis, fever and dehydration aggravate sickling, and should be treated promptly. Prevent acidosis by alkalinising the urine.

Management of Complications

- Hip joint and eye surgery.
- LASER surgery for complications in the eye.
- Treatment of focal neurological deficit by blood transfusion within 1 hour of focal neurological deficits.
- Treatment of acute chest syndrome—consists of oxygen administration (if oxygen saturation is below 90%), and simple exchange blood transfusion (manual or automated).

Prevention of Infection

- Antibiotics—prophylaxis with oral penicillin at least up to 5 years of age and erythromycin ethylsuccinate 10 mg/kg twice daily orally.
- Immunisation with influenza vaccine once a year.

Prognosis

Life expectancy in sickle-cell anaemia is decreased. Few children remain symptom free for years while some develop complications due to progressive tissue and organ damage.

Sickle–Haemoglobin C Disease (Hb SC)

Red blood cells do not polymerise like HbSS but form crystals which lead to dehydration and sickling. Clinical features and complications are similar to HbSS but occur with less frequency. Some of these are as follows:

- Increased incidence of retinopathy
- Chronic hypersplenism
- Splenic sequestration
- Renal medullary carcinoma

Sickle-Cell Trait (HbAS)

The children may be asymptomatic. Blood count is normal. The total amount of HbS in these children is less than 50% of the total Hb. Complications include sudden death during exercise due to splenic infarcts at high altitudes, hyposthenuris, haematuria, becteriuria, renal medullary carcinoma and eye injury with hyphaema formation. Children with sickle-cell trait should not be restricted from normal physical activities. Lifespan is normal.

Antenatal Diagnosis and Genetic Counselling

Antenatal diagnosis is done by polymerase chain reaction (PCR) from the cells obtained by chorionic villi sampling or foetal fibroblasts taken by amniocentesis. The risk of the child is 50% when both parents are carriers. If one of the parents is a carrier the risk is 25%.

Newborn Screening Programme

It is done by the following tests:

- High-performance liquid chromatography
- Thin layer/isoelectric focussing

HEREDITARY SPHEROCYTOSIS (CONGENITAL ACHOLURIC JAUNDICE)

It is an auto-haemolytic anaemia which is usually inherited as autosomal dominant disorder, but may be sporadic (due to new mutations) or inherited as autosomal recessive.

Pathophysiology

There is a molecular defect in the gene that encodes

for skeletal proteins of the cell membrane (spectrin, ankyrin, band 3 protein, etc.). These proteins are responsible for maintaining the normal biconcave shape of the RBCs. In the presence of such defects, the RBCs assume a spherical shape due to loss of membrane. They have difficulty in passing through the spleen. They are, therefore, treated as old and damaged by the spleen. This leads to premature senescence and destruction of RBCs in the spleen.

Clinical Features

Age of onset is in infancy. Clinical features vary in severity. Common clinical features:

- Anaemia
- Jaundice
- Splenomegaly

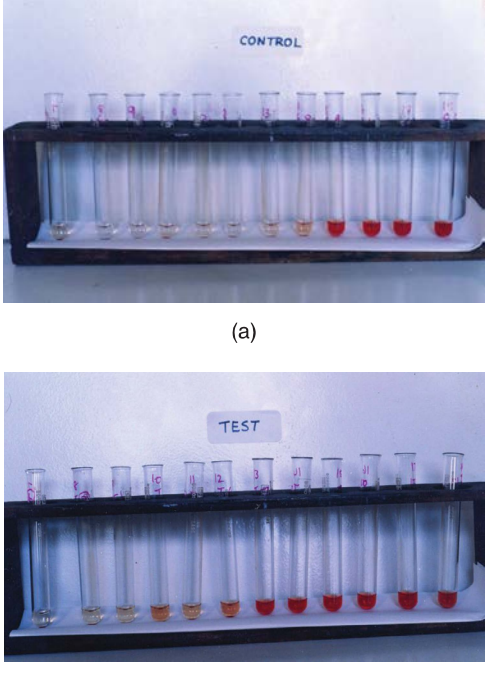
Neonatal anaemia and hyperbilirubinaemia may be severe enough to require phototherapy, blood transfusion or exchange transfusion.

Complications

- Aplastic crisis (usually precipitated by infection with parvovirus)
- Haemolytic crisis
- Gallstones
- Haemochromatosis
- Impaired growth
- Leg ulcers

Investigations

- Complete blood count—decrease in Hb% and MCV; increase in MCHC, RDW; reticulocytosis.
- Peripheral smear—Spherocytes (spherical RBCs which are smaller than normal RBCs and lack central pallor).
- Bone marrow studies—red cell precursors are not spherocytic. Bone marrow shows erythroid hyperplasia.
- Evidence of haemolysis—reticulocytosis, anaemia, hyperbilirubinaemia (hyperbilirubinaemia is unconjugated [hence called acholuric jaundice] with normal liver enzymes).
- Osmotic fragility test—When erythrocytes are suspended in hypotonic solution, they swell due to entry of water and sodium into the cells. When they cannot imbibe more water, they undergo lysis. As the volume of spherocytic RBCs is maximum for its surface area, they cannot swell further and this results in lysis. Varying concentrations of normal saline are used in osmotic fragility test. In normal children, the lysis begins at a saline concentration of about 0.45%–0.50% and completes in 0.30%–0.33%. In patients with hereditary spherocytosis, the lysis occurs at a higher saline concentration of about 0.6% (Fig. 13.7).
- Autohaemolysis test—when blood is incubated under sterile conditions at 37°C for 48 hours, only about 5% of the RBCs haemolyse normally, but in hereditary spherocytosis, about 15%–45% cells haemolyse. This percentage decreases when glucose is added to the solution.
- Direct antiglobulin test—negative; this rules out autoimmune haemolytic anaemia.



(a)

(b)

FIGURE 13.7 Osmotic fragility test. The erythrocytes are suspended in decreasing concentrations of normal saline. (a) Control: in normal children, the erythrocytes are resistant to lysis at higher saline concentration. (b) In hereditary spherocytosis, the erythrocytes cannot swell and lyse at a higher saline concentration.

Differential Diagnosis

1. Other causes of congenital anaemia
2. Acquired spherocytosis is seen in the following conditions:
   - Autoimmune haemolytic anaemia—Coomb's test is positive
   - ABO incompatibility
   - Thermal injury to red cells may result in acquired spherocytosis

Treatment

- Supportive treatment for anaemia and jaundice—phototherapy in the neonatal period, blood transfusions, exchange transfusion.
- Splenectomy—it is the definitive treatment. It should preferably be done after 5–6 years of age (as the risk of postsplenectomy sepsis is high in very young children) but before puberty (when the burden of erythropoiesis increases). It is indicated in a child with impaired growth or frequent aplastic crisis or very severe transfusion dependent disease. The child should be vaccinated with multivalent pneumococcal and haemophilus vaccines prior to surgery. Penicillin prophylaxis should also be given.
- Cholecystectomy may be done at the same time as splenectomy in patients who present with gall stones.

Prognosis

Haemoglobin and reticulocyte count return to normal. Spherocytes persist in the peripheral smear. Thrombosis is common. Osmotic fragility test becomes more pronounced after splenectomy.

COMPLICATIONS OF HAEMOLYTIC ANAEMIA

- Gall stones—Excessive breakdown of the RBCs leads to increased pigment excretion in the bile. This predisposes to tendency for the formation of gallstones.
- Jaundice—It occurs due to haemolysis. Gall stone formation can also cause obstruction of the bile duct and lead to obstructive jaundice.
- Infarctions in various organs such as spleen, lungs (haemoptysis) and kidney (haematuria). The involvement of the fingers leads to pain and gangrene of the fingers and toes.
- Chronic non-healing ulcers—especially on the lower part of the legs near the malleoli. This occurs in sickle-cell anaemia and congenital spherocytic anaemia.
- Acute renal failure—Sudden intravascular haemolysis predisposes to oliguria, anuria and acute renal failure.
- Disseminated intravascular coagulation (DIC)—The intravascular breakdown of RBCs leads to thromboplastic activity. This predisposes to DIC. This abnormal coagulation formation in turn activates the fibrinolytic system.
- Kernicterus—The unconjugated bilirubin can cross the blood–brain barrier, especially in the newborn babies and may get deposited in the brain cells and lead to kernicterus.
- Enlargement of the marrow space—It occurs due to increased erythropoietic activity to compensate for the haemolysis. During childhood the red marrow occupies whole of the skeleton, and there will be no space for expansion. This results in encroachment of the cortex, leading to increase in the diploeic space. The inner and outer tables are thinned out and the space between them is increased. This results in frontal and parietal prominence. The eyes are widely placed, and the bridge of the nose is flattened. The malar bones become prominent. As the soft tissues cannot keep pace with the malar bone enlargement, the upper lip is stretched; the distance between the upper lip and the nose is more. The upper lips cannot cover the upper teeth. Because of the overgrowth of the upper jaw there is malocclusion of the teeth.
- Hypersplenism occurs and requirement of the transfusion increases.
- Haemosiderosis—Normal iron absorption from gut is 1 mg of iron per day. In patients with thalassaemia up to 10 mg of iron per kg will be absorbed. Also 1 mL of the packed cell contains 1–1.6 mg of iron. Iron overload occurs due to increased gastrointestinal iron absorption, repeated blood transfusion and increased

TABLE 13.13 Differentiating Features between Different Types of Haemolytic Anaemia

Features	Beta Thalassaemia	Hereditary Spherocytosis	Sickle-Cell Anaemia
Other name	Cooley anaemia	Acholuric jaundice	Sickle-cell disease
Pathogenesis	Synthesis of β-chains is depressed or absent due to mutation in the β-genes	Defect in the gene that encodes for skeletal proteins of the cell membrane (spectrin, ankyrin, band 3 protein, etc.)	Point mutation in the β-globin gene located on chromosome 11 results in replacement of valine for glutamic acid in the sixth position in the β-polypeptide chain The red cells are sickle shaped and there is increased blood viscosity
Age at onset	Around 6 months of life due to presence of foetal haemoglobin	In infancy Newborns can present with jaundice and kernicterus	Presents at birth but usually present by 2–4 months of age
Clinical features	Progressive pallor Mild jaundice Irregular fever (due to increased metabolic activity)	Jaundice	Fatigue Abdominal pain Bone pain Jaundice
	Characteristic haemolytic facies Skeletal changes Hepatosplenomegaly	Anaemia Splenomegaly	Splenomegaly in early stages, later atrophy Clubbing
Severity of anaemia	Severe anaemia	Mild anaemia	Mild anaemia
Reticulocyte	10% or more	5%–20%	5%–15%; Reticulocytopenia during aplastic crisis
RBCs	Microcytic Hypochromic	Diameter decreased Spherocytosis—decreased diameter Reduction in surface area Decreased surface area to volume ratio Volume normal or slightly decreased Rigid red cells	Sickle-shaped red blood cells
Peripheral smear	Target cells Microcytes Hypochromic anaemia	Spherocytes	Sickle cells, anisocytosis poikilocytosis, Howell–Jolly bodies, target cells
Red cell indices	MCV decreased MCH decreased MCHC decreased	MCV normal or slightly decreased MCHC increased MCH normal	Normocytic, normochromic MCV normal MCH normal
Hb electrophoresis	HbA normal HbA2 and HbF increased	Haemoglobin normal	HbS
Osmotic fragility test	Decreased osmotic fragility	Greatly increased osmotic fragility	Decreased osmotic fragility
Radiological changes	Widening of medulla Thinning of cortex X–ray of skull—hair on end appearance	Extra medullary hemapoiesis –paraspinal swelling circumscribed, lobulated mass on the posterior mediastinum	Skull—ground glass or hair-on-end appearance. Long bones may show cortical thickening and patchy irregularities. Expanded marrow spaces and osteoporosis
Expansion of bone marrow	Expansion of bone marrow	Moderate expansion of bone marrow as compared to thalassaemia	Expansion of bone marrow
Treatment	Blood transfusion, stem cell transplantation	Splenectomy	Packed-cell transfusion for aplastic crisis or sequestration Prevention of complications

haemolysis. Deposition of iron in various organs leads to various complications.

- It predisposes to endocrinopathies such as hypoparathyroidism (hypocalcaemia, hyperreflexia, seizures and tetany), hypogonadism/gonadal failure (delayed puberty), hypothyroidism and diabetes mellitus.
- Hepatic iron concentration >15 mg/g weight is a risk factor for cardiac rhythm disturbances and cardiac failure.
- The complexion of the child is greyish due to the deposition of the iron in the skin.
- Iron deficiency anaemia can be caused by haemoglobinuria, which results in loss of iron from the body.
- Relative folic acid deficiency due to increased folate consumption and megaloblastic anaemia can occur.
- Infections due to poor resistance to infections. Repeated blood transfusions increase the risk for infections such as hepatitis and HIV.
- Nerve compression—Extramedullary erythropoiesis can lead to enlargement of the bones, which results in symptoms due to pressure on the adjacent structures.

Differentiating features between different types of haemolytic anaemia are given in Table 13.13.

BLEEDING DISORDERS

Primary haemostasis is defined as the formation of the primary platelet plug and involves platelets, the blood vessel wall and von Willebrand factor (vWF). Secondary haemostasis is defined as the formation of fibrin through the coagulation cascade. Based on the abnormality in either the platelets or the coagulation cascade, there are two major patterns of bleeding disorders (Table 13.14).

- Abnormal platelets
- Abnormal coagulation cascade

Type of bleeding helps differentiate between platelet disorders and coagulation disorders. Platelet disorders manifest as skin bleeds like purpura and ecchymoses or mucosal bleeds like gum bleeds and epistaxis. The defect is in the initial haemostatic mechanism. The bleeding manifestation occurs throughout the body. Coagulation disorders are usually present with deep bleeds such as haematomas and haemarthrosis. Prolonged bleeding at the site of injury will be present.

TABLE 13.14 Bleeding Disorders

Features	Abnormal Platelets (Primary Haemostasis)	Abnormal Coagulation Cascade (Secondary Haemostasis)
Site of bleeds	Mucous membrane	Deep sites
Common sites	Epistaxis, haematuria, petechiae, GIT bleeds, menorrhagia	Bleed into muscles, joints Ecchymosis, haematomas

HISTORY TAKING

Age

Various bleeding disorders present in different age groups.

- Newborn—haemorrhagic disease of newborn, factor XIII deficiency, isoimmune thrombocytopenia, congenital amegakaryocytic thrombocytopenia
- Infancy—thrombocytopenia with absent radius (TAR) syndrome presents in infancy
- Toddler—haemophilias, von Willebrand disease (vWD) and Ehlers–Danlos syndrome
- Acute idiopathic thrombocytopenic purpura (ITP) usually presents by 1–4 years of age
- Chronic ITP presents after 10 years

Sex

Haemophilia, Wiskott–Aldrich syndrome are X-linked recessive disorders and are common in males. SLE and chronic ITP are more common in girls.

Presenting Complaints

- Bleeding from the injured site for a longer time than usual
- Spontaneous bleeding
- Bleeding from gums—spontaneous or while brushing
- Bleeding per rectum

- Passing black tarry stools
- Blood in vomiting

History of Present Illness

- Ask if the bleeding is spontaneous or after injury. Ask about the site of bleed, duration, number of episodes, amount of bleed, onset, frequency, precipitating or relieving factors. Ask about the severity of bleed—whether or not it could be tolerated, or did it require blood transfusion, etc.
- GI bleeds may manifest as haematemesis, melena or haematochezia
- H/o bleeding diathesis (deficiency of vitamin K)—abnormal prolonged bleeding from injured sites, bleeding from normal sites, bleeding from gums spontaneously or while brushing the teeth
- H/o abdominal pain, bone pain, arthritis, arthralgia (leukaemia)
- H/o fever
- H/o haematuria
- H/o black-coloured urine in black water fever (malaria)
- H/o jaundice (liver disorders)
- H/o oedema (due to hypoproteinaemia in liver disorders)
- H/o nausea/vomiting (uremia)
- H/o gastroenteritis (HUS)
- H/o steatorrhoea (malabsorption of fat predisposes to vitamin K deficiency)

History of Past Illness

Enquire about past episodes of bleeding at the injured sites or spontaneous bleeding.

Treatment History

- H/o transfusions
- Treatment with drugs such as steroids for ITP
- Drugs predisposing to thrombocytopenia—aspirin, anticoagulants, β-lactum antibiotics and chloramphenicol

Antenatal History

- H/o drug intake
- H/o Rh incompatibility
- Maternal ITP associated with neonatal thrombocytopenia
- Intrauterine infections such as rubella, CMV, toxoplasmosis, congenital syphilis cause increased platelet destruction

Birth History

- H/o excessive bleeding during birth

Neonatal History

- Excessive bleeding from any site
- Bleeding from the umbilical stump

Nutritional History

- Dietary history to find out vitamin C and vitamin K deficiency

Immunisation History

- H/o bleeding from injection sites

Personal History

If the child is above 7 years, ask if the child is playful.

History of Allergy and Contact

H/o allergy—skin, nasal, respiratory and gastrointestinal allergies should be enquired. Any allergy to food or drugs should be enquired. Cow's milk allergy is associated with gastrointestinal bleeding.

Family History

- History of bleeding disorders in other family members
- Ask if only males are affected (haemophilia)
- H/o menorrhagia in any family member (vWD)

Social and Environmental History

Exposure to toxin and chemicals may result in aplastic anaemia. The history taking should be followed by detailed physical examination of the child.

GENERAL EXAMINATION

- Dysmorphic features
- Absent thumb—TAR syndrome
- Thumb hypoplasia/aplasia (Fanconi's anaemia)

Vital Signs

- Pulse—increased in acute blood loss
- Respiratory rate—increased in children with bleeding severe enough to cause anaemia
- Heart rate—increased in acute blood loss
- Blood pressure—decreased in severe bleeding
- Temperature—elevated in infections. Temperature is decreased in severe sepsis which may predispose to DIC

Anthropometry

- Weight—decreased in severe malnutrition
- Midarm circumference—decreased in malnutrition

SYSTEMIC EXAMINATION

Examination of Nervous System

Higher functions may be altered in CNS bleeds.

Examination of Abdomen

- Hepatomegaly
- Splenomegaly

Examination of Cardiovascular System

TAR syndrome is associated with TOF and ASD.

THROMBOCYTOPENIA

Thrombocytopenia is a condition associated with decreased platelet count. Common causes are

- Premature destruction of platelets
- Decreased production of platelets
- Trapping of platelets in an enlarged spleen

Classification

I. Quantitative disorders

1. Primary thrombocytopenia (acute/chronic)—It occurs due to decreased production of platelets. Causes are as follows:
   (a) Congenital—TAR syndrome, Wiskott–Aldrich syndrome, Chediak–Higashi syndrome, Bernard–Soulier syndrome
   (b) Acquired—Bone marrow infiltration (leukaemia, neuroblastoma, histiocytosis and so on)
2. Secondary thrombocytopenia
   (a) Sequestration—Hyperthermia, hypothermia
   (b) Dilution of blood—Massive transfusion
   (c) Increased destruction
   - Immunological ITP—Drug induced, infective, posttransfusion purpura, autoimmune disorders, vWD type II b, alloimmune disorders
   - Non-immunological—HUS, DIC, Kasabach–Merritt syndrome

   (d) Increased consumption—Renal vein thrombosis, giant haemangioma, HUS, DIC, HELLP syndrome
   (e) Decreased production and increased destruction
   - Infection—TORCH
   - Erythroblastosis foetalis
   - Osteopetrosis

II. Qualitative disorders—Thrombasthenia (weak platelets). It is an inherited autosomal recessive disorder of platelet function, which includes deficiencies of platelet adhesion, aggregation and secretion. It is characterised by a lifelong bleeding tendency. The production and assembly of the platelet membrane glycoprotein (GP) IIb–IIIa is altered, preventing the aggregation of platelets and subsequent clot formation.

Causes

Causes according to the frequency of occurrence are as follows:

1. Common causes
   - Acute and chronic ITP
   - Drugs (digoxin, sulphonamides, salicylates, chlorthiazides, quinidine, phenobarbitone)
   - Chemicals (pesticides, arsenic and benzene can slow the production of platelets)
   - Leukaemia
   - Bone marrow infiltration—myelosclerosis, secondaries, malignant lymphomas
   - Aplastic anaemia
   - Hypersplenism
   - SLE
2. Less common causes
   - Infections
   - DIC
3. Rare causes—thrombotic thrombocytopenic purpura

IDIOPATHIC THROMBOCYTOPENIC PURPURA

It is an autoimmune disorder characterised by antibody-mediated destruction of platelets. It is a self-limiting disorder, which usually resolves spontaneously within a few months of onset. Incidence is 4 to 8 per 1000 children per year. It can occur at any age.

Pathogenesis

Autoantibodies against platelet antigens are formed after infection with EBV, varicella, influenza, parvovirus B19 and HIV. These antibodies coat the platelets. The antibody coated platelets bind to Fc receptors in the splenic macrophages and are destroyed. Spleen is central in both formation of antibodies and destruction of platelets. The onset of the disease is seen about 1–4 weeks after the infection.

Types

- Acute self-limiting ITP
- Chronic ITP

Acute ITP

Clinical Features

- Sudden onset of petechiae or purpura in the previously well child (commonest manifestation) (Fig. 13.8)
- Haemorrhage may be mild or severe
- Mucous membrane bleeding —epistaxis, gingival bleeding
- Bleeding in internal organs—gastrointestinal bleeds. Intracerebral bleeding is rare
- First manifestation may be menorrhagia at the menarche

Investigations

- Thrombocytopenia
- Hb, WBCs normal
- Bone marrow normal

Treatment

Aim of treatment is to prevent life-threatening bleeding and to prevent anaemia from prolonged bleeding. Treatment consists of the following measures:

- Prednisolone is given in a dose of 1–4 mg/kg/day for 2–3 weeks and then tapered. Steroids cause more rapid rise in the platelet count. They increase the lifespan of the platelets and maintain the capillary integrity. They also decrease the severity and shorten the duration of the initial phase.



FIGURE 13.8 A child with ITP. Note the purpuric spots on cheeks, ecchymosis on forehead and haemorrhage in the tongue.

- In severe cases, methyl prednisolone 30 mg/kg/day for 3 days can be used. This drug causes a more rapid rise in platelets.
- Intravenous immunoglobulin (IVIG) 1 g/kg for 2 days, followed by 400 mg/kg/day for 5 days. This increases the platelet count within 24–48 hours. Immunoglobulin competes with the IgG-sensitised platelets for the Fc binding sites on the monocytes and macrophages. This also acts by production of anti-antibodies which in turn binds to the circulating autoantibodies and suppresses B cells which produce antibodies.
- If there is relapse, booster IV IgG 1 g/kg or intravenous methyl prednisolone is useful.
- Splenectomy is indicated in cases of life-threatening bleeding not responding to medical treatment.
- Plasma exchange is useful if the patient does not respond to IVIG or splenectomy.
- Platelet transfusion is useful in life-threatening haemorrhages. The lifespan of the transfused platelets can be prolonged by prior infusion of γ-globulin.
- Supportive measures—These consist of restriction of physical activities, avoidance of intramuscular injections and drugs such as aspirin which impair the platelet functions. If anaemia is present, transfusion is needed.

Prognosis

Remission occurs in 2–8 weeks. Few cases may last for 6 months or persist as chronic ITP.

Chronic ITP

It is common in females above the age of 10 years. The platelet count persists below 100,000 cells/mm^3 for 6 months or more. Onset is less abrupt and symptoms are usually mild.

Clinical Features

Symptoms last for more than 6 months. These are

- Petechiae or ecchymosis
- Severe bleeding from the mucous membrane (localised to one site)
- Recurrent epistaxis, haematuria and menorrhagia
- Splenomegaly

Course of Illness

Symptoms are intermittent or may be persistent but fluctuate in severity.

Investigations

- Tourniquet test or Hess test
- Platelet count—decreased
- Clot retraction time—prolonged
- Coagulation time—normal
- Anaemia
- WBC count; ESR is normal
- Bleeding time—prolonged (measurement of the cessation of haemorrhage from a small puncture wound under standard conditions [Ivy's method])
- Bone marrow—normal or increased number of megakaryocytes and their precursors

Treatment

1. IVIG
2. Corticosteroids
3. Splenectomy—spleen is the main site for the production of antibodies and destruction of antibody-coated platelets. If the bleeding is refractory to IV IgG, splenectomy should be performed. The platelet count starts rising immediately after the splenectomy. Splenectomy predisposes to certain infections. Antibiotic prophylaxis should be continued. Immunisation against pneumococcus *H. influenzae,* meningococci should be administered
4. Immunosuppressive drugs—cytotoxic drugs are given in resistant cases
   - Azathioprine—1–2 mg/kg/day
   - Cyclophosphomide—1–2 mg/kg/day
   - Cyclosporine
5. Androgens—Danazol, 300–400 mg/m^2
6. Anti-Rh D induces mild haemolytic anaemia. This results in blockage of RE cells by sensitised RBCs. This is useful in Rh negative patients only
7. Anti-Fc-receptor monoclonal antibody and dapsone may also be tried

Differences between acute and chronic ITP are given in Table 13.15.

TABLE 13.15 Differences between Acute and Chronic ITP

Features	Acute ITP	Chronic ITP
Onset	Acute	Insidious
Age	2–6 years	Older age
Sex incidence	Equal	Females > Males
Antecedent infection	Common	Unusual
Platelet count	<20,000/mm^3	30,000–80,000 cells/mm^3
Duration	4–6 weeks	>6 months
Spontaneous remission	Common	Not common
Associated findings	Eosinophilia, lymphocytosis	Immunological abnormalities
Treatment	Steroids	Steroids Immunosuppressive drugs Splenectomy

HAEMOPHILIA

It is a bleeding disorder which occurs due to deficiency of coagulation factors.

Types

1. Congenital
   - Haemophilia A (factor VIII deficiency)—commonest
   - Haemophilia B (factor IX deficiency)
   - Haemophilia C (factor XI deficiency)
2. Acquired—occurs due to autoimmune depletion of clotting factors

Genetics

Haemophilia A and B are inherited as X-linked traits. They occur because of mutations in the long arm of chromosome X. They occur commonly in males due to X-linked recessive inheritance. However, they can occur in females in the following cases:

- Lyonisation of X chromosome
- Turner's syndrome
- Spontaneous autosomal translocation disruption structure of factor VIII or factor IX gene

Haemophilia C has autosomal inheritance.

Grading of Severity

The severity of haemophilia A and B is graded on the basis of levels of coagulation factor VIII and factor IX, as given in Table 13.16. Normal plasma level is 100 IU/dL or 100%. The lower limit of normal levels of factor VIII and IX is approximately 50%. The haemostatic level for factor VIII is >30–40 IU/dL, and for factor IX is >25–30 IU/dL. Haemophilia C is much less common and less severe. Severity of bleeding does not correlate with levels of factor XI.

Clinical Features

These vary according to the age. The disease usually remains undiagnosed in the newborn period.

Newborn

- Cephalhaematoma
- Intracranial bleeds
- Profuse bleeding following circumcision

Early Infancy

- Easy bruising
- Prolonged bleeding from minor trauma

Late Infancy and Childhood

Symptoms usually appear when the child begins to cruise. These are as follows:

- Haemarthrosis—ankle is involved early followed by knee joint
- Intramuscular bleeding

TABLE 13.16 Grading of Severity of Haemophilia A and B

Grading of Severity	Clotting Factor Activity (%)	Clotting Factor Level (IU/dL)	C/F
Mild haemophilia	>5	>5	Often goes unnoticed till significant trauma occurs
Moderate haemophilia	1–5	1–5	Bleeding occurs with mild trauma
Severe haemophilia	<1	<1	Spontaneous bleeding

- Intracranial bleeding
- Haematuria
- Gastrointestinal bleeding
- Frequent bleeding—more than two episodes of bleeding in the same joint per month. Complications of frequent bleeding include cartilage destruction, narrowing of joint space, chronic haemophilic arthropathy

Investigations

1. PTT—prolonged
2. Assay for factor VIII, IX and XI
3. Factor-specific antibodies in patients with previous infusion of factors

Treatment

Haemophilia A and B

1. The aim of treatment is to raise the factor level to 35–50 IU/dL in mild-to-moderate bleeding and 100 IU/dL in severe bleeding. This is done by factor replacement. Factor VIII concentrates contain 250–500 units of factor VIII. Calculation of dose of factor VIII and IX is as follows:

$$\text{Total dose of factor VIII (IU)} = \text{weight (kg)} \times \text{\%rise desired} \times 0.5$$

$$\text{Total dose of factor IX (IU)} = \text{weight (kg)} \times \text{\%rise desired} \times 1.4$$

   Frequency of administration is based on half-life. Half-life of factor VIII is 12 hours. Half-life of factor IX is 18–24 hours. One unit of factor VIII raises the factor VIII level by 2%. One unit of factor IX raises the factor IX level by 1.5%.
2. Prophylactic factor therapy should be given if the factor level is less than 1%.
3. If factors are not available, fresh frozen plasma or cryoprecipitate can be given.
4. If inhibitors are present, non-factor-based therapy such as desmopressin can be given in patients with mild haemophilia A.
5. Supportive care.

Haemophilia C

Factor XI concentrates are not available, so fresh frozen plasma is used for treatment of haemophilia C along with supportive care.

Prevention

Prevention includes antenatal diagnosis by DNA analysis.

VON WILLEBRAND DISEASE

It is inherited as an autosomal dominant disease. Chromosome 12 contains gene for vWF. Functions of vWF are as follows:

1. vWF binds to the subendothelial matrix and causes platelets to adhere.
2. Helps in platelet aggregation.
3. Acts as a carrier protein for plasma factor VIII.

Classification

1. Hereditary
   - Classical—type I, II and III
   - Pseudoplatelet type of vWD
2. Acquired

Hereditary vWD

1. *Classical vWD* is of three types.
   (a) *Type I:* Quantitative defect in vWF. The vWF is decreased. It is the most common and mildest form of disease.
   (b) *Type II:* Qualitative defect in vWF. The vWF is abnormal. It is of two types
      - Type IIA—multimers are smaller than normal.
      - Type IIB—deficiency of binding of vWF to factor VIII.

   (c) *Type III:* Total absence of vWF, severe variety.
2. *Pseudo-vWD or platelet type of vWD* is inherited as autosomal dominant and is similar to type IIB vWD but the defect is in the platelet and not in the factor. There will be mutation of the vWF receptor on the platelets. The abnormal receptor, GP Ib will display an increased affinity for vWF.

Clinical Features

Bleeding manifestations may present as

- Epistaxis

- Mucocutaneous bleeding
- Ecchymoses over back, shoulder and thigh
- Prolonged bleeding following tonsillectomy or tooth extraction
- Girls—menorrhagia

Positive family history of bleeding is present

Acquired vWD

It is due to the presence of a factor which results in rapid clearance of vWF from the plasma. Following are the conditions associated with acquired vWD:

- Hypothyroidism
- Wilms tumour
- Systemic lupus erythematosus
- Infections such as Ebstein barr virus
- Drugs—valproate therapy, ciprofloxacin

Clinical Features

- Late-onset bleeding
- No family history of bleeding

Investigations

- Bleeding time prolonged
- Platelet count is normal
- vWF antigens
- Structure of vWD is altered
- Activated partial thromboplastin time (APTT) prolonged
- Ristocetin aggregation is absent or decreased and will get corrected by adding plasma

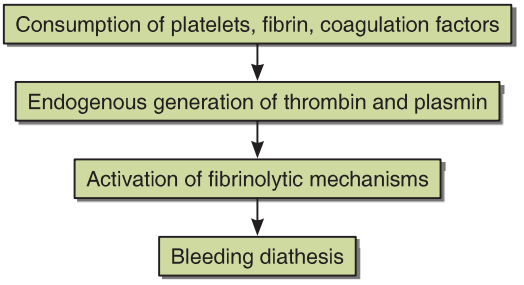
Treatment

- Desmopressin 0.3 µg/kg intravenously. This should be infused in 30–50 mL of normal saline over 20–30 minutes. Desmopressin acetate (DDAVP) can also be given by intranasal route in a dose of 150 µg for children weighing less than 50 kg
- Cryoprecipitate
- Plasma-derived vWF concentrate 1 U/kg will raise its activity by 1.5–2.0 IU/dL (1.5%–2.0%)

DISSEMINATED INTRAVASCULAR COAGULATION

Disseminated intravascular coagulation is a condition which is characterised by diffuse fibrin deposition in the microvessels, resulting in intravascular activation of coagulation, depletion of clotting factors and end-organ damage.

Pathogenesis



Types of DIC

1. Acute—sepsis, burns
2. Chronic—acute promyelocytic leukaemia, retention of dead foetus

Conditions Associated with DIC

- Infections—sepsis
- Neoplasms—acute promyelocytic leukaemia, etc.
- Burns
- Trauma
- Snake bite
- Shock
- Severe transfusion reactions
- Rheumatologic illness
- Severe hepatic failure

Clinical Features

- Bleeding from sites of injection
- Petechiae/ecchymoses

- Epistaxis
- Gingival bleeding/mucosal bleeding
- Cough/dyspnoea
- Confusion, disorientation
- Fever
- Tissue necrosis

Investigations

- Peripheral smear—thrombocytopenia, microangipathic haemolytic anaemia
- Prothrombin time prolonged
- APTT prolonged.
- D-dimer assay is the most sensitive test—elevated
- Assay for fibrin degradation products—elevated

Treatment

Acute DIC

- Treat the underlying cause
- Restoration of clotting factor
- Fresh frozen plasma
- Cryoprecipitate
- Platelet transfusion

Chronic DIC

Heparin infusion can be given in chronic DIC along with the above given management.

CHAPTER 14

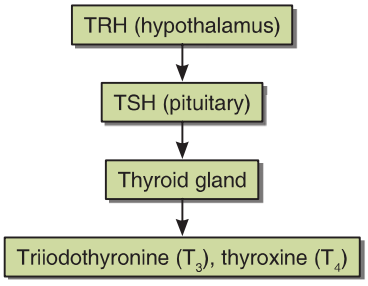
Disorders of Endocrine System

HYPOTHYROIDISM

Hypothyroidism refers to the deficiency of thyroid hormones and is one of the common preventable causes of mental retardation.

PHYSIOLOGY OF THYROID GLAND

The thyroid gland secretes hormones T_3 and T_4 in response to thyroid-stimulating hormone (TSH) from the pituitary gland. The secretion of TSH is in turn controlled by thyrotropin-releasing hormone (TRH) secreted from hypothalamus.



The normal values of thyroid hormones and TSH vary according to age. These are shown in Table 14.1.

CLASSIFICATION

Hypothyroidism can be classified into primary and secondary.

Primary Hypothyroidism

The defect in the thyroid gland leads to an increase in TSH. The causes are as follows:

1. Congenital
   (a) Dysgenesis/agenesis of thyroid gland (the most common cause is hypoplastic glands)

TABLE 14.1 Normal Values

Age	Reference Range
TRH (pg/mL)	
All ages	5–60
TSH (mIU/mL)	
Preterm (first week)	0.7–27.0
Term (first week)	1.0–38.9
2–20 weeks	1.7–9.1
5 months–18 years	0.7–6.4
Level of free T_4 (ng/dL)	
0–3 days	2–4.9
Infants	0.9–2.6
1–10 years	0.8–2.2
>10 years	0.8–2.3
Level of free T_3 (pg/dL)	
Newborn (cord blood)	20–240
1–3 days	200–610
3 days–6 weeks	240–560
Children and adults	230–660

(b) Dyshormonogenesis—defective thyroid hormone synthesis
(c) Inherited defects in the thyroid hormone receptors—insensitivity to thyroid hormones
(d) TRH unresponsiveness (mutations in receptors)
(d) Maternal medication with propylthiouracil, carbimazole, radionucleotide iodine, methimazole and amiodarone

2. Acquired
(a) Iodine deficiency
(b) Goitrogenic food intake such as soyabeans, pine nuts, peanuts and strawberries
(c) Autoimmune diseases such as Graves' disease and Hashimoto's thyroiditis
(d) Polyglandular syndromes
(e) Iatrogenic
- Drug induced—iodides, propylthiouracil and carbimazole
- Irradiation
- Surgical ablation

Secondary Hypothyroidism

This condition occurs because of a decrease in the secretion of TSH, which may be due to a defect in the pituitary gland (hypopituitarism) or because of a decrease in the secretion of TRH, which may be due to a defect in the hypothalamus.

Differentiating features between primary and secondary hypothyroidism are shown in Table 14.2.

TABLE 14.2 Differentiating Features between Primary and Secondary Hypothyroidism

S.N.	Features	Primary	Secondary
1	Incidence	More common	Less common
2	Skin	Thick and without wrinkles	Thin with fine wrinkles
3	Hair	Coarse	Fine
4	Menstrual irregularities	Menorrhagia more common	Amenorrhoea more common
5	Secondary sexual characters	Normal	Poor
6	Heart size	May be enlarged	Small
7	Goitre	May be present	Absent
8	Soft tissue oedema	Marked	Absent
9	Blood pressure	Normal or high	Low
10	Associated features	Not significant	Midline defects, hypoglycaemia secondary to GH deficiency, ACTH deficiency, microphallus, hypoplastic scrotum, undescended testes
11	Cholesterol	Increased	Normal
12	TSH	High	Low
13	Plasma cortisol	Normal	Low
14	TRH stimulation test	Exaggerated response	No response
15	Thyroid autoantibodies	May be present	Absent

HISTORY TAKING

Age

Congenital hypothyroidism is seen in newborns and goiter due to iodine deficiency is seen in the pubertal age group.

Sex

Hypothyroidism is common in girls.

Place

Endemic goiter is common in hilly areas (because of iodine deficiency).

Presenting Complaints

- Intolerance to cold
- Constipation

History of Present Illness

- Oedema
- Intolerance to cold
- Impairment of hearing
- Delayed dentition
- Poor school performance
- Hoarse cry/noisy breathing
- Muscle weakness (proximal muscles)
- Mood swings
- Weight gain
- Decreased appetite
- Depression
- Short stature
- Early or late sexual development
- Lethargy
- Excessive sleepiness

History Pertaining to Aetiology

- H/o similar illness in mother
- H/o drug intake
- H/o surgery in the neck
- H/o irradiation

Antenatal History

- Drug intake—iodine, radioiodine, antithyroid drugs (propylthiouracil and carbimazole), amiodarone, cough expectorants and antimalignant drugs. When given antenatally these can cause hypothyroidism in an infant.
- H/o decreased foetal movements

Birth History

- Hoarse cry after birth

Neonatal History

- Prolongation of physiological jaundice
- Delayed passage of meconium
- Constipation since birth
- Lethargy

Family History

- Any other family member having similar illness
- H/o goiter (Fig. 14.1)

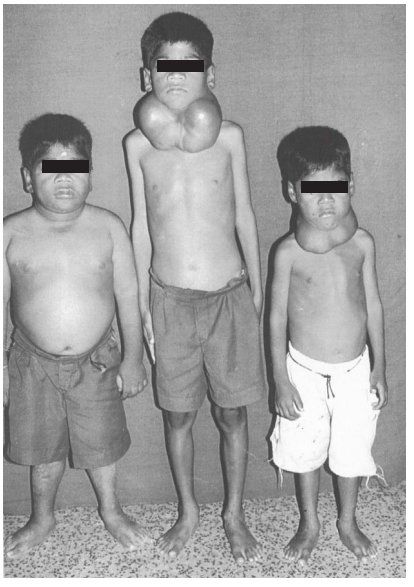


FIGURE 14.1 Familial hypothyroidism. Three siblings presented with thyroid swelling and features of hypothyroidism.

- Pendred syndrome due to deficiency of peroxidase enzyme is associated with deafness

CLINICAL EXAMINATION

General Examination

- Mental retardation (Fig. 14.2)
- Growth retardation
- Disproportionate short stature (infantile variety)
- Weight gain and oedema
- Lethargy
- Hypothermia

Head-to-Toe Examination

1. Head
   - May be large due to myxoedema of brain
   - Microcephaly
   - Delayed closure of anterior and posterior fontanels
2. Face
   - Characteristic coarse facies (Fig. 14.3)
   - Forehead covered with hair



FIGURE 14.2 Hypothyroidism with mental retardation.

3. Eyes
   - Narrow palpebral fissure (due to myxoedema of eyelids)
   - Widely separated eyes
   - Oedema of eyelids
   - Synophrys (eyebrows meet in the midline)
4. Nose—Broad with flattened bridge
5. Oral cavity
   - Open mouth (due to large tongue)
   - Macroglossia
   - Delayed dentition
6. Neck
   - Short and broad (due to deposits of fat above the clavicles)
   - Thyroid swelling (Fig. 14.4)
7. Hair
   - Coarse, brittle or scanty
   - Sparse outer one-third of the eyebrows
8. Skin
   - Dry, myxoedematous, sallow complexion
   - Thick, cold and clammy skin
   - Vitiligo (white spots on the skin)

Systemic Examination

Cardiovascular System

- Bradycardia (sleeping pulse rate is low)
- Cardiomegaly (pericardial effusion)

Respiratory System

- Breathing difficulties (due to large tongue)



(a) (b)

FIGURE 14.3 Child with hypothyroidism. (a) Before treatment. (b) After treatment. Note the return of smile after treatment.



(a) (b)

FIGURE 14.4 Thyroid swelling. (a) Normal position. (b) Moves up on swallowing.

Gastrointestinal System

- Protuberant abdomen
- Umbilical hernia (Fig. 14.5)

Central Nervous System

- Mental retardation—the growth of the brain mainly occurs in the first 3 years. Any deficiency of the thyroid hormones at this age results in mental retardation.
- Speech slurred
- Hoarse voice
- Impaired hearing
- Carpal tunnel syndrome (compression of the median nerve)
- Ankle jerk with delayed relaxation phase (pseudomyotonic reflex)



FIGURE 14.5 Hypothyroidism in a 2-year-old child. The child has coarse facies, macroglossia, umbilical hernia and short stature.

Musculoskeletal System

- Weakness of muscles (endocrine myopathy)
- Hypotonia

Haematological System

- Iron deficiency anaemia refractory to treatment with iron

CONGENITAL HYPOTHYROIDISM

Clinical Features

- Letharginess
- Feeding difficulties
- Nasal obstruction and apnoea
- Prolongation of physiological jaundice (due to delayed maturation of the glucoronide conjugation)
- Constipation (delayed passage of meconium)
- The weight and the length are normal at birth
- Posterior fontanel may be open (due to delayed skeletal maturation in utero)

TABLE 14.3 Quebec Scoring

No.	Clinical Stigmata	Scoring
1	Feeding problems	1
2	Constipation	1
3	Lethargy	1
4	Hypotonia	1
5	Coarse facies	3
6	Macroglossia	1
7	Open posterior fontanel	1.5
8	Dry skin	1.5
9	Mottling of skin	1
10	Umbilical hernia	1
Total		13

- Anterior fontanel wide open
- Skin—dry, thick, coarse, cool and mottled

As it is difficult to diagnose hypothyroidism in newborns, Quebec scoring has been devised (Table 14.3). If the score is >4/13, hypothyroidism is suspected and the child is investigated accordingly. This is important as early diagnosis and intervention can prevent mental retardation.

Investigations

Screening of TSH levels in the blood taken 5–7 days after birth.

Treatment

Replacement therapy with L-thyroxine should be started as early as possible in a dose of 10–15 µg/kg/day for neonates and should be continued lifelong (Table 14.4).

TABLE 14.4 Recommended Daily Dosage of L-Thyroxine

Age	Dose (µg/kg/day)
0–3 months	10–15
3–6 months	8–12
6–12 months	6–8
1–5 years	4–6
5–12 years	3–5
>12 years	2–4

Response to Therapy

After the treatment begins in a neonate, it takes 1 month to normalise T_4 with a dose of 8–10 µg/kg, whereas it takes a week to normalise T_4 with a dose of 10–15 µg/kg. The serum TSH level takes 3–6 months to come down to normal.

Prognosis

- The treatment should be started at the earliest to avoid irreversible brain damage. Delayed diagnosis and replacement therapy will lead to the development of mental retardation.
- The decreased levels of thyroid hormone in the young age result in a condition called cretinism.

Follow-up

Child should be monitored for thyroid hormone levels and TSH monthly in the first 6 months, then every 2–3 months between 6 months to 2 years of age. Follow-up includes growth and development assessment, radiological assessment, laboratory assessment and psychometric assessment.

ACQUIRED HYPOTHYROIDISM

When the level of thyroid hormones decreases after a period of normalcy, it is called acquired hypothyroidism. It results in myxoedema in which there is an infiltration of mucopolysaccharidosis (hyaluronic acid and chondroitin sulphate) in many body tissues.

Clinical Features

- Growth retardation
- Delayed dentition
- Myopathy
- Delayed or absent sexual maturation
- Menorrhagia
- Impotency in adults
- Myxoedema (eyelids, dorsal aspect of hands, below and above the clavicles, over the tendons, entrapment neuropathy)
- Kocher–Debre–Semelaigne syndrome—generalised pseudohypertrophy of muscles gives a Her-

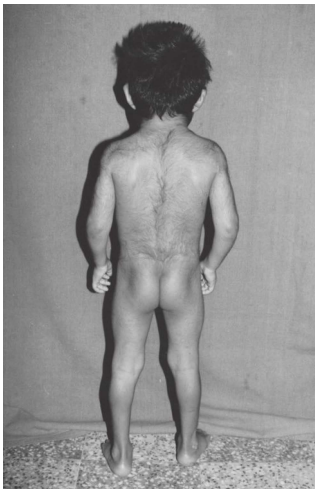


FIGURE 14.6 Generalised pseudohypertrophy of muscles: Kocher–Debre–Semelaigne syndrome.

culean appearance in long-standing cases. It is also known as myopathy of hypothyroidism (Fig. 14.6).

Investigations

1. Thyroid hormone studies—serum levels of T_3, T_4 (free and total) and TSH.
2. X-ray—the following radiological changes can be seen in a child with hypothyroidism.
   (a) Delayed skeletal maturation.
   (b) Delayed formation of upper tibial, lower femoral and cuboidal epiphysis in neonates (Box 14.1).
   (c) Changes in wrist—delayed formation of carpel bones.
   (d) Changes in the skull—brachycephaly, wormian bones, delayed dentition, wide sella, wide anterior fontanel, sutural separation, small occipital and parietal bones, osteosclerosis and delayed development of paranasal sinus.
   (e) Changes in the vertebral column—wide intervertebral space.
3. Blood smear—normocytic normochromic anaemia.
4. Thyroid scan—radioactive iodine uptake test.
6. Thyroid ultrasound.
7. Serum thyroid binding globulin (TBG).
8. Electroencephalogram (EEG)—shows delta waves shows and increased amplitude.

BOX 14.1 Differential diagnosis for absent lower femoral epiphysis at birth

At 36 weeks in 96% of the infants the epiphysis at the lower end of the femur appears; by 40 weeks the upper tibial epiphysis appears. However, it may be absent at birth in some normal children and in children with IUGR, prematurity, cretinism and intrauterine infections (except syphilis).

Treatment

Older children require 4–8 µg/kg/day of L-thyroxine (Table 14.4). It is given lifelong once a day, early morning on an empty stomach. Side effects are rare and occur usually due to overdosage. These include anxiety, agitation, diarrhoea, weight loss or gain, excessive sweating, flushed skin, tiredness, palpitations, tachycardia, wide pulse pressure (increased risk of CCF and arrhythmia), chest pain, tremors, insomnia, hyperactivity irritability, excitability, nervousness and craniosynostosis.

In older children, side effects include pseudotumour cerebri (benign intracranial tension) and temperomental problems.

Follow-up

The follow-up includes clinical, laboratory, radiological and psychometric assessment of the child. Follow-up is scheduled initially 15 days after starting the treatment, then monthly till 6 months, then once in 3 months, then once in 6 months and finally once a year.

1. Clinical assessment
   - Growth monitoring—monitor weight, height, head circumference and chest circumference.
   - Monitor developmental milestones.
2. Laboratory assessment—thyroid function tests are done on first and fourth week after starting therapy; then after every 1–2 months during the first year; then after every 3 months in second

and third year. (TSH level <10 μIU/mL indicates effective therapy.)
3. Radiological bone age assessment—it is done for skeletal maturation.
4. Psychometric assessment—it is done for early identification of children with low IQ.

ADRENOCORTICAL INSUFFICIENCY

Adrenocortical insufficiency is a condition in which the production of one or more adrenal gland hormones is either decreased or absent.

PHYSIOLOGY OF ADRENAL SECRETION

The adrenal gland is composed of the adrenal cortex and the adrenal medulla. On the basis of histology, the adrenal cortex is divided into three zones—zona glomerulosa, zona fasciculata and zona reticularis. Each of these is associated with the synthesis of specific hormones. The zona glomerulosa synthesises aldosterone, zona fasciculata synthesises cortisol, and zona fasciculata and reticularis synthesise androgens (Table 14.5).

Corticotropin–releasing hormone (CRH) secreted from the hypothalamus acts on the pituitary gland. Adrenocorticotropic hormone (ACTH) or corticotropin secreted by the pituitary acts on the adrenal gland, which secretes cortisol, aldosterone and androgens (Fig. 14.7). Any defect in this pathway results in decreased production of adrenal hormones. The cortisol in the blood will have a negative feedback on the secretion of ACTH by the pituitary. An increase in cortisol results in decreased secretion of ACTH and vice versa.

TABLE 14.5 Adrenal Steroid Hormones

Hormones	Synthesis	Regulation of Secretion
Cortisol (glucocorticoid)	Zona fasciculata	Mainly by ACTH from anterior pituitary
Aldosterone (mineralocorticoid)	Zona glomerulosa	Mainly by renin–angiotensin system and potassium levels. Short-term effect by ACTH
Androgens	Zona fasciculata and reticularis	Complex mechanisms not completely understood

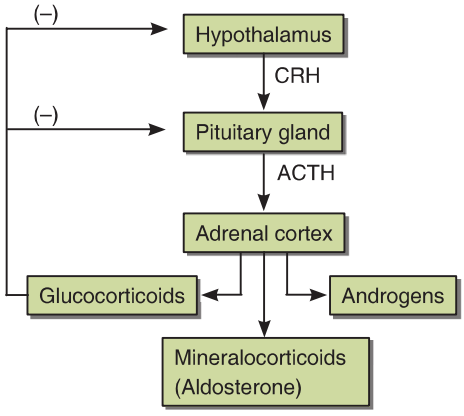


FIGURE 14.7 Physiology of adrenal secretion.

CLASSIFICATION

Adrenocortical insufficiency can be classified into the following types:

I. Primary—due to defect in adrenal glands.

II. Secondary—due to defect in the pituitary resulting in decreased production of ACTH.

III. Tertiary—due to defect in the hypothalamus resulting in decreased production of CRH.

Primary Adrenal Insufficiency

It occurs due to destruction or decreased function of adrenal cortex. There is an impaired production of cortisol, and often aldosterone, despite normal or increased ACTH. It can be genetic or acquired. The causes are as follows:

1. Autoimmune adrenalitis—isolated or part of autoimmune polyendocrinopathy (APS)
2. Infectious adrenalitis—bacterial (tuberculosis), fungal (cryptococcosis, histoplasmosis) and viral (HIV, CMV)
3. Genetic disorders
   - Adrenoleukodystrophy (ALD)

- Congenital adrenal hyperplasia (CAH)
- Adrenal hypoplasia congenita

4. Bilateral adrenal haemorrhage—meningococcemia (Waterhouse–Friedrichson syndrome)
5. Adrenal infiltration—sarcoidosis, amyloidosis and haemochromatosis
6. Bilateral adrenalectomy
7. Drug-induced adrenal insufficiency—ketoconazole, rifampicin, anticonvulsants (phenytoin and phenobarbitone), mitotane

Acquired primary adrenal insufficiency is termed as **Addison's disease.** It results from autoimmune causes, infections, drugs and haemorrhage in the adrenals.

Secondary Adrenal Insufficiency

It is more common than primary adrenal insufficiency. Pituitary causes of failure to produce ACTH are

- Pituitary tumours—craniopharyngioma, microadenoma
- Pituitary infarction—Sheehan's syndrome
- Pituitary haemorrhage
- Granulomatous infiltration—sarcoidosis
- Congenital hypopituitarism
- Abrupt cessation after prolonged administration of corticosteroids—suppression of hypothalamic –pituitary–adrenal axis (HPA)

Tertiary Adrenal Insufficiency

It occurs due to defect in the hypothalamus resulting in decreased production of CRH. The causes are as follows:

- Head injury
- Radiation
- Surgery
- Infections—meningitis

CLINICAL FEATURES

These depend on the age of the patient and whether both aldosterone and cortisol are deficient and up to what extent. Infants have an acute presentation and the prominent signs are due to hyperkalaemia, hyponatraemia and hypoglycaemia. In older children, the onset is gradual and these may be easily misdiagnosed as gastroenteritis or other infections.

1. Due to glucocorticoid deficiency
   - Hypoglycaemia
   - Ketosis
   - Anorexia, nausea, vomiting and diarrhoea/constipation
   - Orthostatic hypotension, which may progress to shock
   - Electrolyte abnormalities—hyponatraemia
   - Muscle weakness, malaise, myalgia, fever, weight loss and easy fatigability
   - Disorientation and depression
   - Pallor, hypercalcaemia, eosinophilia and lymphocytosis
2. Due to mineralocorticoid deficiency
   - Hypotension
   - Electrolyte abnormalities—hyponatraemia and hyperkalaemia
   - Craving for salt
3. Due to increased ACTH secretion—hyperpigmentation in sun-exposed areas, pressure areas such as elbow and knee, palmar creases, knuckles, mucous membranes, conjunctiva.
4. Due to decreased adrenal androgen—decreased body hair. This is more marked in females with hypopituitarism

INVESTIGATIONS

1. Blood tests—haemoglobin (anaemia), total count and differential count (eosinophilia, lymphocytosis).
2. Blood pH—decreased due to metabolic acidosis.
3. Serum electrolytes—hyponatraemia, hyperkalaemia and hypercalcaemia.
4. Blood glucose—decreased.
5. Serum cortisol and ACTH levels—in primary adrenal insufficiency, cortisol levels are low in the presence of increased ACTH. In secondary or tertiary insufficiency, both are either decreased or at the lower end of normal (Table 14.6).
6. ACTH stimulation test—it measures the adrenal responsiveness to administration of ACTH. Serum cortisol should be measured before and 60 minutes after the administration of ACTH.

TABLE 14.6 Serum Cortisol and ACTH Levels in Primary and Secondary Adrenal Insufficiency

Types of Adrenal Insufficiency	Plasma ACTH	Serum Cortisol
Primary	Increased	Decreased
Secondary or tertiary	Normal or decreased	Normal or decreased

It helps to differentiate between primary and secondary or tertiary adrenocortical deficiencies. Serum cortisol is increased in secondary and tertiary adrenocortical insufficiency, whereas in primary adrenocortical insufficiency there is no increase.

7. Overnight metyrapone test—it is a simple test to determine the function of the HPA axis. Single dose of metyrapone 30 mg/kg is given at 11 pm and levels of cortisol, ACTH and 11-deoxycortisol are measured at 8.00 am. Normally, the levels of ACTH and 11-deoxycortisol should increase; however, no or impaired response is seen in pituitary and hypothalamic disease.
8. CRH stimulation test—it is done when ACTH stimulation test is abnormal. CRH 1 μg/kg is administered intravenously in bolus at 9 am. Twenty-four hour blood samples for cortisol and ACTH are collected 15 minutes immediately before and 5, 15, 30, 60, 120 and 180 minutes after CRH. Normally, ACTH peaks 30 minutes after CRH and serum cortisol peaks at 60 minutes. In secondary insufficiency, ACTH and cortisol response are decreased or absent. CRH will not stimulate the pituitary if it is damaged. In children with Addison's disease, high levels of ACTH but no increase in cortisol occurs. In hypothalamic disease, prolonged ACTH responses and abnormal cortisol responses are seen.
9. Ultrasonography and CT scan of abdomen are also done.

TREATMENT

Primary Adrenal Insufficiency

1. Replace both glucocorticoids and mineralocorticoids
   (a) Glucocorticoids
   - Prednisolone—3.5 mg/day/m^2
   - Hydrocortisone 25–30 mg in infants and 50–75 mg in older children (at every 6 hours for 24 hours). If the condition of the child improves the dose can be decreased.
   - Cortisone acetate

   (b) Mineralocorticoids—fludrocortisone
2. Antibiotics
3. Antituberculous treatment (4 HRZE/6 HR) should be given if evidence of tuberculosis is present

Secondary and Tertiary Adrenal Insufficiencies

- Replace only the glucocorticoids. If any other pituitary hormones are deficient they may be given.
- In cases of HPA axis suppression, give the steroids and then taper it slowly. Give the drug daily for 2 weeks and then on alternate days. Then the dose can be tapered slowly. Once the dose of prednisolone is decreased to 5 mg/kg/day, add hydrocortisone (20–25 mg/kg/day).

COMPLICATIONS

- Severe hypotension
- Shock
- Adrenal crisis (Box 14.2)

Differences between primary, secondary and tertiary adrenal insufficiency are shown in Table 14.7.

CONGENITAL ADRENAL HYPERPLASIA

This is a congenital disorder of biosynthesis of adrenal corticosteroids (cortisol, aldosterone or both).

PATHOGENESIS

Various enzymes are involved in the synthesis of adrenal corticosteroids. Deficiency of any of these enzymes results in decreased production of

BOX 14.2 Adrenal crisis

It occurs due to sudden cessation of hormone secretion by the adrenal gland. It is more common in Addison's disease. Precipitating factors are stress-like accident, injury, surgery, severe infection, fluid loss (diarrhoea) and sudden withdrawal of steroids in children who are on long-term steroids.

Clinical features include nausea, vomiting, abdominal pain, fever, somnolence and hypovolaemic shock (poor capillary refill)

Treatment of adrenal crisis:

- Hypoglycaemia and hyponatraemia should be corrected
- Hydrocortisone (at 6 hours for 24 hours) should be given
- Fludrohydrocortisone in a dose of 0.05–0.1 mg should be given
- Normal saline should be given
- Dopamine infusion for hypotension
- Treatment of the predisposing cause
- Salt intake should be adequate

cortisol (Fig. 14.8). This causes increased secretion of ACTH, thereby stimulating the adrenal cortex, but due to a defect in the pathway, cortisol is not produced. However, there is an increase in the intermediate metabolites such as deoxycortisone (which has salt-retaining action similar to that of aldosterone) and DHEA (which has androgenic activity half that of testosterone). Depending on the metabolite that is increased, a range of clinical features are seen.

ENZYME DEFICIENCIES

Common enzyme deficiencies seen are

- 21-Hydroxylase deficiency (>90% of cases)
- 11β-Hydroxylase deficiency
- 3β-Hydroxysteroid dehydrogenase
- Cholesterol desmolase
- 17β-Hydroxyl steroid dehydrogenase

TYPES

- Salt-losing variety—the commonest cause of CAH is 21-hydroxylase deficiency.
- Salt-retaining variety—it occurs due to either 11β-hydroxylase deficiency or 17-hydroxylase deficiency.

CLINICAL FEATURES

These depend on the enzyme that is deficient in the steroidogenesis pathway. The common clinical features are as follows:

- Ambiguous genitalia in females and infantile genitalia in males (Fig. 14.9)
- Female pseudohermaphroditism—hypertrophy of clitoris
- Postnatal virilisation
- Pubic and axillary hair may appear at an earlier age than expected
- Progressive weight loss, anorexia, vomiting, dehydration, hypotension, hypoglycaemia, hyperkalaemia and hyponatraemia in salt-losing variety

TABLE 14.7 Differences between Primary, Secondary and Tertiary Adrenocortical Deficiencies

Features	Primary	Secondary	Teritiary
Site of lesion	Adrenal gland	Pituitary	Hypothalamus
Pathogenesis	Destruction of adrenal glands	Decreased ACTH secretion, adrenals are intact	Decreased CRH secretion, adrenals are intact
Hormones	Both cortisol and aldosterone decreased	Aldosterone not affected, may be associated with hypothyroidism and hypogonadism	Aldosterone not affected, may be associated with other endocrine problems
Hyperpigmentation	Present	Absent	Absent
Plasma ACTH level	High	Low	Low
Treatment	Replace both glucocorticoids and mineralocorticoids	Replace glucocorticoids, treat associated conditions such as hypothyroidism	Glucocorticoids

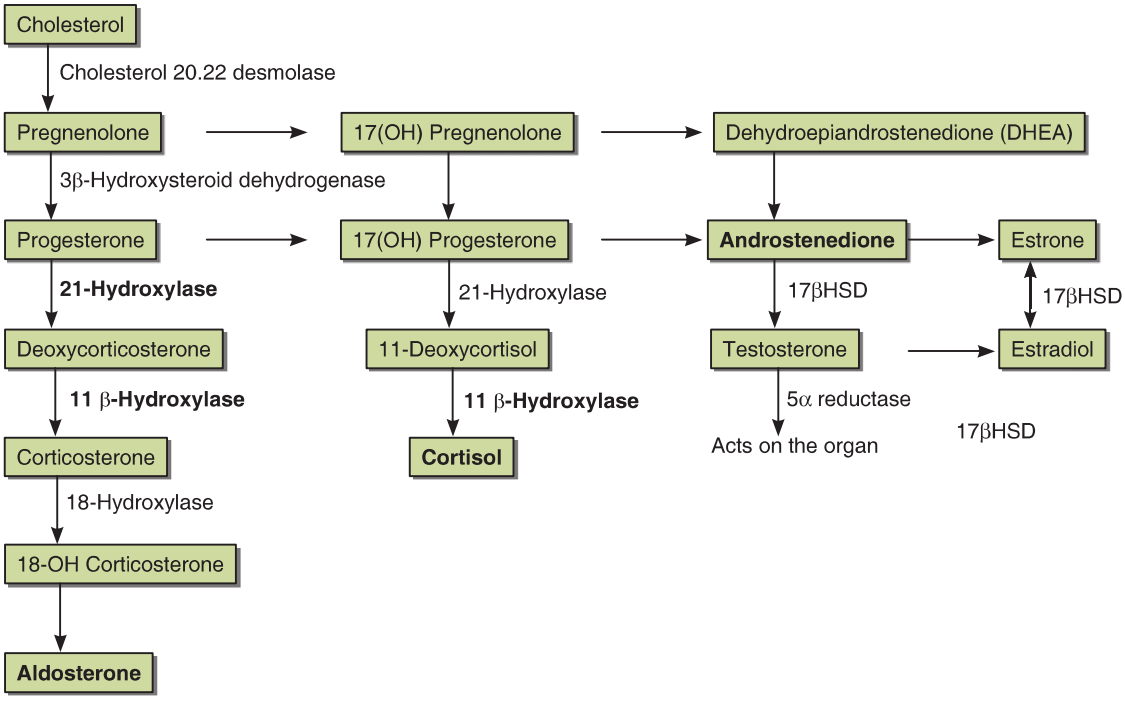


FIGURE 14.8 Steps in synthesis of adrenal corticosteroids.

- Tall stature in childhood
- Elevated blood pressure in salt-retaining type of CAH



FIGURE 14.9 Ambiguous genitalia.

INVESTIGATIONS

- Plasma levels of 17 ketosteroids and 17 (OH) progesterone are elevated
- Elevated levels of 17 (OH) progesterone following ACTH are seen in 21-hydroxylase deficiency
- High levels of androstenedione and testosterone in females, or in adolescent males
- Deoxycorticosterone and 11-deoxycortisol are elevated in 11β-hydroxylase deficiency
- Serum electrolytes—low sodium and high potassium levels in salt-losing type
- Radiological—advanced bone age
- Karyotyping to ascertain the sex of the child
- Antenatal diagnosis is done by chorionic villi sampling in the first trimester and detection of 17 (OH) progesterone in amniotic fluid in the second trimester

TREATMENT

The aim of treatment is to decrease the rate of bone growth, stop virilisation, prevent salt loss and to attain normal puberty by glucocorticoid and mineralocorticoid replacement and surgical correction of ambiguous genitalia.

Medical Treatment

- Glucocorticoid replacement—hydrocortisone is given in a dose of 20–25 mg/m^2/day orally in two or three divided doses. Prednisolone may also be given in some cases.
- Mineralocorticoid replacement—it is given in salt wasting variety of CAH. Fludrocortisone is given in a dose of 0.1–0.3 mg/day in early infancy. In later infancy and childhood, dose required will be 0.05–0.1 mg daily.

Surgical Treatment

Genitoplasty or clitoroplasty is done for surgical correction of ambiguous genitalia.

Antenatal Treatment

Treatment in the antenatal period is done by administration of dexamethasone 1.5 mg/day in two or three divided doses.

COMPLICATIONS

- Bilateral testicular tumours
- Adenomatous change in the adrenal gland

CUSHING'S SYNDROME

It occurs because of excess of glucocorticoid levels in the body due to either exogenous administration or excess endogenous production by the adrenal cortex.

AETIOLOGY

1. Exogenous causes—intake of steroids such as prednisolone, dexamethasone and methylprednisolone has the same effect as endogenous cortisol production.
2. Endogenous causes—overproduction of cortisol may be due to excess production by adrenal gland or excess ACTH production which regulates cortisol production. The causes are as follows:
   - Benign tumour of pituitary gland—it is the most common cause of Cushing's syndrome and is called Cushing disease.
   - Ectopic ACTH secreting tumour—it may be benign or malignant and occurs in lungs, pancreas, thyroid and thymus gland.
   - Disorders of adrenal gland—it includes primary adrenal gland diseases which are ACTH independent. Common form is adrenal adenoma.

CLASSIFICATION

Cushing's syndrome can be classified into the following types:

I. ACTH-independent Cushing's syndrome

1. Adrenal adenoma—benign adenoma
2. Malignant tumours in the adrenal cortex—these secrete androgens in addition to cortisol
3. Adrenal hyperplasia—micronodular or macronodular

II. ACTH-dependent Cushing's syndrome

1. Cushing disease—excess ACTH secretion by a pituitary adenoma causes bilateral adrenal hyperplasia
2. Ectopic ACTH secreting tumours
   - Ectopic ACTH secreting tumours are seen in pancreas, lungs and thyroid. Examples include oat cell carcinoma, small cell carcinoma and carcinoid tumour.
   - Rarely ectopic CRH secretion results in increased ACTH secretion causing Cushing's syndrome.

CLINICAL FEATURES

Adrenal gland tumours and pituitary tumours are more common in females. Ectopic ACTH production

is common in males. The clinical features are as follows:

- Obesity involving upper body with thin arms and legs (sparing of extremities); buffalo hump (fatty hump between the shoulders); fat deposition over cheeks, chin, upper trunk and interscapular area.
- Plethoric and moon facies—rounded, red face (cushingoid facies) (Fig. 14.10).
- Short stature.
- Skin—violaceous pink or purple striae over the abdomen, buttocks, lower back, upper thighs, upper arms and breasts; ecchymoses; thin and fragile skin that bruises easily; cutaneous atrophy with exposure of subcutaneous vessels; skin infections.
- Acne, hirsutism and hypertrichosis (signs of abnormal masculinisation).
- Fatigue, proximal muscle weakness, backache, bone pain and tenderness and osteoporosis.
- Mental changes—depression, anxiety, irritability, and behavioural changes.
- Cushing disease—hypertension, hyperglycaemia, acne, weight gain, fatigue, muscle weakness, facial flushing, loss of emotional control, decreased libido in adolescents and adults, erectile dysfunction in males, irregular or absent menstruation in girls and hirsutism.



FIGURE 14.10 Cushingoid facies due to exogenous intake of steroids in a child with steroid-dependent nephrotic syndrome.

DIFFERENTIAL DIAGNOSIS

Pseudo-Cushing's syndrome

This is seen in patients with depression or alcohol abuse. The clinical and biochemical findings are similar to Cushing's syndrome. Both have elevated urinary free cortisol. The findings resolve when the primary condition is treated.

Dexamethasone–CRH test is done to differentiate between mild Cushing's syndrome and pseudo-Cushing states. This test combines the two tests—low-dose dexamethasone suppression test and the CRH stimulation test. In patients with Cushing's syndrome, dexamethasone is not able to suppress the production of pituitary ACTH. CRH stimulates production of ACTH and thereby cortisol levels. In Cushing's syndrome, there is larger increase in plasma ACTH and cortisol levels than in pseudo-Cushing states.

Eight doses of 0.5 mg dexamethasone are given every 6 hours starting at 12 noon. This is followed by the administration of CRH intravenously after 2 hours of the last dose of dexamethasone. Plasma cortisol and ACTH should be measured at 15-minute interval for 1 hour. Plasma cortisol level greater than 1.4 μg/dL is seen in Cushing's syndrome and values less than that are seen in pseudo-Cushing states.

INVESTIGATIONS

Baseline Investigations

- Blood sugar—elevated
- Serum electrolytes—potassium levels are low (especially in patients with ectopic secretion of ACTH)
- Arterial blood gas analysis—metabolic acidosis (due to activation of renal mineralocorticoid receptor by the cortisol)

Investigation to Confirm Cushing's syndrome

- Diurnal cortisol tests—there is a loss of circadian rhythm of cortisol (and ACTH) levels in Cush-

ing's syndrome resulting in elevated night-time plasma and salivary cortisol levels. (Normally cortisol levels are high in morning and fall at midnight.)

- Dexamethasone suppression test—patients with Cushing's syndrome are resistant to suppression by low-dose dexamethasone. A dose of 25–30 µg/kg (maximum 2 mg) of dexamethasone is administered orally at 11 pm. A cortisol level less than 5 µg/dL at 8 am, the next morning, is seen in normal children. A level below 1.8 µg/dL excludes Cushing's syndrome.
- 24-hour urinary free cortisol—this is expressed as a ratio of amount of cortisol (in micrograms) excreted per gram of creatinine. Urinary free cortisol levels are three- to fourfold increased in patients with Cushing's syndrome.

Investigation to Diagnose Complications

- X-ray adsorptiometry (DEXA) for bone density may indicate osteoporosis.
- Serum cholesterol—high level of cholesterol and triglycerides, low level of high-density lipoprotein.

Investigation to Find Out the Cause of Excess Cortisol Production

- Serum ACTH and cortisol levels—both are increased in ACTH-dependent lesions; cortisol alone is increased in serum and urine in ACTH-independent lesions.
- Effect on ACTH and cortisol levels in response to intravenous administration of CRH—levels are elevated in patients with ACTH-dependent Cushing's syndrome; no increase is seen in ACTH-independent lesions.
- Two-step dexamethasone suppression test—dexamethasone is administered in doses of 30 and 120 µg/kg/day in four divided doses for two consecutive days. Only the larger dose suppresses the serum cortisol levels in Cushing disease (pituitary tumour), whereas no suppression with any of the doses occurs in ACTH-independent lesions.

Investigations to Find Out the Site of Tumours

- X-ray of skull—look for enlargement of sella turcica, which is seen in pituitary tumours
- Ultrasound of abdomen
- CT scan of brain, chest and abdomen
- MRI of skull, chest and abdomen

MANAGEMENT

Treatment may be medical or surgical according to the cause.

Exogenous Cushing's syndrome

One should stop administration of the steroids and substitute with other drugs if the child is on treatment with steroids. If it is not possible to stop steroids, complications should be monitored by checking blood glucose, cholesterol and X-ray for osteoporosis.

Endogenous Cushing's syndrome

Surgical removal of tumour secreting cortisol or ACTH should be done.

1. Pituitary tumours (Cushing disease)
   - Trans-sphenoidal pituitary microsurgery should be done to remove the tumour. Adenomectomy or hypophysectomy can also be done. This is followed by pituitary irradiation or re-operation in relapse cases.
   - Bilateral adrenalectomy can be done if pituitary surgery is not possible. Nelson syndrome is seen after adrenalectomy in unresected pituitary adenoma. It occurs due to increased ACTH secretion and causes marked hyperpigmentation.
   - Replacement therapy with hydrocortisone is required lifelong after removal of the tumour.
2. Adrenal tumour
   - Adrenal adenoma may be removed surgically. Unilateral or subtotal adrenalectomy should be done, as required.

- Medical adrenalectomy involves the use of adrenal enzyme inhibitors which act by decreasing the cortisol secretion. These include metyrapone (11-β-hyroxylase inhibitor), aminoglutethimide (which blocks the conversion of cholesterol to pregnenolone), adrenolytic agents (mitotane) and ketoconazole (blocks 20, 22 desmolase).
- Mifepristone, an antiprogestational agent that binds with glucocortiocoid and progesterone receptors in high doses, is under trial.

3. Ectopic ACTH secreting tumours
   - Inhibition of steroidogenesis—ketoconazole and metyrapone.
   - Adrenalectomy—in refractory cases.
   - Pre- and postoperative replacement therapy with corticosteroids is required in patients undergoing adrenalectomy.

COMPLICATIONS

- Metabolic—hyperglycaemia and kidney stones.
- Musculoskeletal system—loss of muscle mass and strength, pathological fractures due to osteoporosis.
- Mental changes—psychosis.
- Endocrine—panhypopituitarism and diabetes mellitus.
- High risk of adrenal crisis—adrenal insufficiency manifesting as low blood pressure and loss of consciousness.
- Adrenal carcinoma can present with virilisation (hirsuitism and male pattern baldness) in women or feminisation in men. Acne may be present over face, chest and back.
- Miscellaneous—frequent infections, growth retardation in children, hypertension, delayed healing of wounds, sodium and water retention (due to cortisol activation of mineralocorticoid receptor) and peptic ulcers.

Complications in Cushing disease

- Headache
- Nocturia and polyuria (due to damage to neurohypophysis resulting in diabetes insipidus)
- Visual problems (due to compression of optic chiasma)
- Galactorrhoea (when the anterior pituitary tumour compresses the pituitary stalk resulting in increased prolactin levels due to loss of dopamine inhibition)
- Irregular menstrual cycles and decreased fertility in females (interruption of LHRH resulting in inhibition of pulsatile secretion of LH and FSH)
- Decreased libido and impotency in males (decreased production of gonadotrophic hormones or LHRH)
- Virilisation in females
- Pressure effects (hyposomatotropism, hypothyroidism, hyperprolactinaemia, hypogonadism)
- Psychological problems (depression, cognitive dysfunction and emotional lability).

PROGNOSIS

There is complete recovery after surgical removal of the tumour. The prognosis of ectopic Cushing's syndrome depends upon the type of the tumour.

HPA axis is suppressed by glucocorticoids. The recovery of HPA axis takes about 1 year after stopping steroids or removal of ACTH- or cortisol-secreting tumour. The steroids should be given at times of stress in patients receiving adrenal steroid inhibitors. If steroids are not given, adrenal crisis may precipitate.

CHAPTER 15

Chromosomal Disorders

DOWN'S SYNDROME (MONGOLISM)

Down's syndrome is named after *Langdon Down* who first described it in 1866. It is the most common autosomal trisomy. Chromosome 21 is one of the smallest human chromosomes. It contains blue print for various proteins, enzymes and other metabolic substances. The extra chromosome 21 results in the excess of some genetic products, thus leading to numerous metabolic imbalances.

INCIDENCE

The disease incidence has been estimated to be 1 in 800–1000 newborns. At conception, the rate is more. Down's syndrome is one of the most common causes of mental retardation.

GENETICS

There is a complete or partial duplication of chromosome 21. The extra chromosome 21 may be of maternal or paternal origin. Following are the causes of Down's syndrome:

1. *Meiotic non-disjunction of chromosome 21*—most common (94%). Meiotic non-disjunction may produce an extra copy of chromosome 21 in egg (95% cases) or sperm (5%). In most cases, the origin is maternal, especially when the mother is older than 35 years. Predisposing causes include increased maternal age, radiation, viral infections, genetic predisposition and environmental toxins.
2. *Translocation*—4%. Chromosome 21 translocates into another chromosome. Majority of translocations are due to translocation involving the chromosomes 13, 14, 15, 21 and 22. The genetic material from one chromosome is replaced by the other. For example, in 14;21 (Robertsonian) translocation, the long arm of chromosome 21 is attached to chromosome 14. Fifty percent translocations are inherited from translocation carrier parent, whereas 50% arise de novo. The common translocations are as follows:
   - 14;21 (commonest)
   - 21;21
   - 13;21
   - 22;21
3. *Mosaicism (normal and abnormal cell lines)*—1%. The defect occurs in the second, third or fourth cell division. Therefore, the cells from the first line are normal. This results in a mixture of normal

cell lines (46 chromosomes) with abnormal ones (47 chromosomes). An abnormal clone is introduced such that the phenotype contains both abnormal and normal cell lines.

4. *Partial trisomy*—only a part of the long arm of chromosome 21 is present in triplicate.
5. *No visible chromosomal abnormality*. Rare

RISK FACTORS

1. Maternal factors—when the maternal age of conception is less than 30 years, translocation is the most common cause of Down's syndrome. When maternal age is more than 30 years, meiotic non-disjunction is more common.
2. Genetic factors—rearrangement of genetic material may occur between chromosomes 14, 21 or 22, in either of the parents. Some of these chromosomes are replaced by the extra chromosome 21. This translocation may be inherited. Either of the parents may be a carrier.

HISTORY TAKING

Complaints

- Delayed milestones
- Recurrent respiratory infections
- Motor clumsiness

History of Present Illness

- Lethargy
- Delayed motor milestones
- Mental retardation
- Delayed dentition

History Related to Other Abnormalities

1. Cardiovascular system
   - Dyspnoea (congestive cardiac failure and cardiac defects)
2. Gastrointestinal tract
   - Vomiting (duodenal atresia)
   - Constipation (Hirschsprung's disease and hypothyroidism)
   - Delayed dentition
3. Central nervous system (CNS)
   - Lethargy
   - Excessive sleepiness (hypothyroidism)
   - Seizures
4. Haematological system
   - Bone pains, gum bleeds, purpura and bleeding from other sites (leukaemia)
5. Miscellaneous
   - Impaired hearing (due to recurrent otits media)
   - Impaired vision (due to cataract)
   - Recurrent respiratory infections (immunodeficiency and hypotonia)
   - Nasal regurgitation of food (due to cleft palate)

Antenatal History

Antenatal history should include the age of the mother at conception.

Birth History

- Flailness at birth (due to hypotonia)

Neonatal History

- H/o prolonged jaundice

Developmental History

- Delay in milestones
- Decreased scholastic performance

Family History

There may be a history of Down's syndrome in siblings.

Personal History

The affected child is playful, loves music, is friendly and enjoys extra attention.

CLINICAL EXAMINATION

General Examination

- Facies—mongoloid facies
- Short stature
- Weak cry
- Intelligent quotient low and mental impairment mild to severe

Vital Signs

Respiratory rate may be increased in the presence of respiratory infections.

Anthropometry

- Height/length—decreased
- Head circumference—microcephaly

FEATURES AT A GLANCE

1. Head
   - Microcephaly
   - Brachycephaly (Fig. 15.1)
2. Face
   - Dysmorphic facies—mongoloid facies (Fig. 15.2)
   - Flat facial profile
   - Flat nasal bridge
   - Mongoloid slant—outer canthus at a higher level than the inner canthus
   - Hypertelorism
   - Brush field spots in iris (speckling of iris)
   - Epicanthic folds of skin extending from the upper lid to cover the medial canthus of eye
   - Small, dysplastic ears (the antihelix is poorly formed, the fossa triangularis and the lobule are absent)
   - Small mouth, protruding tongue, high arched palate and fissured tongue (scrotal tongue)
   - Skin folds at the neck due to abundance of skin there
3. Hands—Dermatoglyphics
   - Simian crease
   - Clinodactyly due to dysplastic middle phalanx of the little finger
   - Brachydactyly—short and stumpy fingers
   - Distal 't' triradius—the meeting of three



FIGURE 15.1. Child with brachycephaly.



FIGURE 15.2. Child with hypertelorism, mongoloid slant and protruding tongue.

dermal ridge patterns (Fig. 15.3)
- Ulnar loops
- Increased 'atd' angle

4. Thorax
   - Short sternum
5. Heart
   - Endocardial cushion defect
   - Ventricular septal defect
6. Pelvis
   - Dysplasia of pelvis
7. Genitalia
   - Small external genitalia
8. Feet
   - Wide gap between the first and the second toes (sandal gap)
9. CNS
   - Mental retardation (mean IQ 50)
   - Developmental delay
10. Musculoskeletal system
    - Hypotonia
    - Cervical spine subluxation
11. Learning problems
    - Cannot write but can read
    - Learning abnormalities—learning difficulties and scholastic backwardness
12. Sexual maturation
    - Secondary sexual characters are delayed

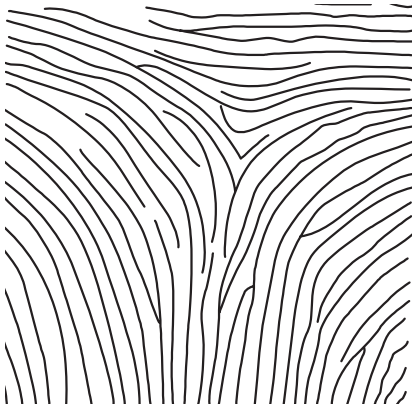


FIGURE 15.3 Triradius.

13. Reproductive system
    - Decreased fertility
    - Males are infertile, but females (fertile) may menstruate and can become pregnant
14. Other features of Down's syndrome
    - Hypothyroidism
    - Leukaemia

Associated problems in case of neonates and older children are given in Box 15.1.

BOX 15.1 Associated problems in case of down's syndrome

Neonates

1. Diseases associated with the gastrointestinal system
   - Duodenal and anal atresia
   - Hirschsprung's disease
   - Tracheo-oesophageal fistula (TEF)
   - Imperforate anus
2. Prolonged jaundice, the causes of which are as follows
   - Annular pancreas (obstructs the bile flow)
   - Constipation (increases the enterohepatic circulation)
   - Hypothyroidism
   - Intrauterine infections
   - Idiopathic
3. Congenital heart defects
4. Dislocation of hips
5. Congenital hypothyroidism

Older children and adolescents

1. Hypothyroidism
2. Alzheimer's disease
3. Male sterility—low testosterone
4. Cataracts
5. Hearing loss

SYSTEMWISE CLINICAL FINDINGS

1. Cardiovascular system—congenital heart defects are seen in 40%–60% of the children.
   (a) Common defects
   - Endocardial cushion defects (most common)
   - Ventricular septal defect

- Mitral valve prolapse

(b) Less common defects
- Isolated secundum atrial septal defect
- Aberrant (retro-oesphageal) right subclavian artery
- Occasional tetralogy of Fallot

(c) Rarely seen defects—patent ductus arteriosus

2. Respiratory system
   (a) Obstructive sleep apnoea
   (b) Hypoplastic lungs
   (c) Excessive pulmonary lobulation
   (d) Diaphragmatic hernia
   (e) Structural changes—double capillary network on the alveolar wall, alveolar ducts increased in size and number of alveoli decreased
3. Gastrointestinal system
   (a) Fissured tongue
   (b) Atresia—duodenal atresia, biliary atresia, intestinal atresia and anal atresia
   (c) Hirschsprung's disease
   (d) Gastro-oesophageal reflux disease
   (e) Tracheoesophageal fistula
   (f) Pyloric stenosis
   (g) Malabsorption
   (h) Umbilical hernia may be present
   (i) Distension of abdomen (due to hypotonia and divarication of recti)
4. Central nervous system
   (a) Mental retardation (incidence is low in mosaicism; few patients with translocation may be normal)
   (b) Epilepsy—infantile spasms and seizures may be present; these are usually present in association with severe mental retardation
   (c) Aggressive behaviour (stubborn)
   (d) Autistic behaviour
   (e) Sleep disturbances (odd sleeping patterns and daytime sleepiness)
   (f) Hypotonia (Moro's reflex may be absent in the newborn)
   (g) Weak reflexes
   (h) Spinal cord compression (atlantoaxial dislocation is common)
   (i) Alzheimer-like dementia—Alzheimer-like diseases occur after 25 years of age And Alzheimer's disease occurs by the age of 40 years
5. Orthopaedic/skeletal system
   (a) Lax joints
   (b) Atlantoaxial subluxation (10%)
   (c) Flared iliac wings with small acetabular angle resulting in an abnormal ilial index
   (d) Dysplasia of pelvis with shallow acetabular angle, which predisposes to hip dislocation
   (e) Dislocation of hip and patella
   (f) Hallux valgus
   (g) Epiphysiolysis of hip
   (h) Congenital talipes equino varus
   (i) Incomplete fusion of vertebra of lower spine
6. Gait disturbances due to hypotonia
7. Endocrine
   (a) Pituitary—underdeveloped
   (b) Adrenals—hyperplasia of cortex and medulla
   (c) Congenital hypothyroidism
   (d) Diabetes mellitus
   (e) Short stature
   (f) Obesity
8. Immune dysfunction
   (a) Decreased T-cell immunity
9. Myelotoxicity, which occurs due to the following reasons
   (a) Increased purine synthesis, which is coded in chromosome 21
   (b) Greater tetrahydrobiopterin demand
   (c) Increased susceptibility to antifolate agents
10. Haematological system
    (a) Polycythaemia in newborn
    (b) Macrocytosis
    (c) Transient myeloproliferative disorder
    (d) Haematological malignancies—leukaemia (AML/ALL) and lymphoma. The risk is 10–18 times more than that of the normal population. Haematological malignancies associated with Down's syndrome depend upon the age

- Newborn—transient leukaemoid reaction
- Infants—acute non-lymphoblastic leukaemia
- Older children—acute lymphoblastic leukaemia

11. Eyes
    (a) Congenital cataract
    (b) Nystagmus
    (c) Refractive errors
    (d) Strabismus
    (e) Cataract at 25 years of age
12. Skin
    (a) Skin infections
    (b) Palmoplantar hyperkeratosis
    (c) Xerosis
    (d) Seborrhoeic dermatitis
    (e) Cutis marmorata

INVESTIGATIONS

1. To confirm the diagnosis
   (a) Karyotyping—chromosomes are grouped from A to G, depending on the length and position of the centromeres. Length of chromosomes in Group A will be the longest and that of Group G will be the smallest. Karyotyping of parents may reveal if one of the parents is a carrier.

Grouping pattern of chromosomes	
A	1, 2, 3
B	4, 5
C	6–12, X
D	13–15
E	16–18
F	19, 20
G	21, 22, Y

2. To diagnose complications
   (a) Complete blood count
   - Peripheral smear—lymphoblasts in leukaemia

   (b) Radiological findings
   - X-ray of spine—done to rule out atlantoaxial dislocation; it should be done between 3 and 5 years
   - X-ray of chest—done to rule out congenital heart disease. Other findings include two or three ossification centres of manubrium, absence of one pair of ribs and abnormalities of the 12th rib (one visible and one rudimentary; both rudimentary; one not visible other rudimentary; both not visible)
   - X-ray of upper limb—accessory epiphysis at the base of second metaphyseal and clinodactyly
   - Ultrasonography of abdomen, barium meal and barium enema—may be suggestive of micro- and megacolon, ileal or jejunal atresia, malrotation of the bowel and oesophageal or pyloric stenosis
   - X-ray of bones—done preferably of the knee joint and shows delayed bone maturation
   - Cranium—X-ray of the skull may show reduced head size (brachycephaly or brachyoxycephaly) and flattening of occiput
   - Vertebral column—incomplete fusion of arches of the lower portion of the vertebral column
   - X-ray of pelvis—done to rule out dislocation of hip; findings include broad and flared iliac wings, and flat acetabulum with acetabular angle reduced, resulting in an abnormal ilial index

   (c) ECHO for congenital heart defects
   (d) EEG for congenital heart defects
   (e) Blood sugar for diabetes
   (f) Thyroid function tests

MONITORING

Monitoring is required for the following complications:

- Atlantoaxial dislocation
- Diabetes
- Leukaemia
- Seizures

- Obstructive sleep apnoea
- Arthritis

TREATMENT

There is no definite treatment for children with Down's syndrome. It is mainly supportive.

1. Nutritional management
2. Immunisation
3. Visual and hearing assessment and aids
4. Speech therapy
5. Education—assess the child and if needed place the child in special schools
6. Treatment of the associated complications
   - Hypothyroidism—thyroxine replacement
   - Congenital heart defects—surgical correction
   - Respiratory infections—antibiotics
   - Seizures—anticonvulsants
   - Orthopaedic problems—physiotherapy
7. Genetic counselling—the parents are counselled regarding the risk of recurrence in the family (Table 15.1) and the facilities available for prenatal diagnosis
8. Anticipatory guidance should be given to the parents regarding the diagnosis, natural history of the disease, course of illness and the complications that the child can develop as he grows

TABLE 15.1 Risk of Recurrence of Down's Syndrome due to Chromosomal Aberrations

Karyotype of the Affected Child	Father	Mother	Chance of Recurrence (%) in the Next Child
Translocation D/G	Normal Carrier	Carrier Normal	10–15 5
Translocation 21/22	Normal Carrier	Carrier Normal	10–15 5
Translocation 21/21	Normal Carrier	Carrier Normal	100 100
Trisomy 21	Normal	Normal	1
Translocation or mosaic	Normal	Normal	<1

COURSE OF THE DISEASE

Presenile dementia is common. Intellectual functions show a decline with age. There is an association of Down's syndrome with Alzheimer's disease. (Neuropathology of both the conditions is similar.)

PROGNOSIS

With the help of advanced medical, educational, emotional and vocational support, these children can lead a semidependent life. Life expectancy is about 50 years.

FOLLOW-UP

These children should be followed at regular intervals (Table 15.2).

TABLE 15.2 Follow-up at Various Ages

Age	Tests
1 month	Eye examination for refractive error/cataract
6 months	Eye examination for refractive error
12 months	Eye examination for refractive error Thyroid function tests
1–10 years	Audiogram Dental examination X-ray cervical spine
11–17 years	Yearly thyroid function tests Yearly ear examination Eye examination Psychiatric evaluation

SCREENING

Indications for screening and diagnostic tests in mother and foetus are as follows:

- Maternal age >35 years
- Previous child with Down's syndrome
- Translocation carrier state in parents
- History of genetic defects in family

Tests for screening are as follows:

1. *Antenatal ultrasonogram*—abdomen and pelvis. Down's syndrome screening programme, based upon second trimester ultrasound, detects only

40% of foetuses with Down's syndrome

(a) First trimester ultrasound screening using a measurement of nuchal translucency (NT): NT is thought to be due to excess nuchal fluid accumulation in a Down's syndrome foetus. NT has been shown to be a powerful indicator of increased risk of aneuploidy (21) and significantly better than second-trimester ultrasound. NT to screen for Down's syndrome consistently achieves a detection rate of approximately 80% and a false-positive rate of 5%. Characteristic features suggestive of Down's syndrome are as follows:
- Short femur and humerus
- Thick nuchal fold (approximately 6 mm) at 16 weeks' gestation
- Polyhydramnios
- Duodenal atresia
- Cardiac abnormality

(b) Second trimester ultrasound screening
- Duodenal atresia
- Cardiac anomalies
- Cerebral ventriculomegaly
- Nuchal oedema
- Pyelectasis (dilation of the renal pelvis)
- Echogenic bowel
- Shortened femur

2. *Triple test* (16 weeks)—done on maternal blood. Characteristic features suggestive of Down's syndrome are the following:
   (a) Decreased α-fetoprotein (α-fetoprotein is estimated between 16 and 20 weeks of pregnancy. Second trimester maternal serum α-fetoprotein in pregnancies with Down's syndrome foetus are, on average, decreased)
   (b) Decreased unconjugated oestriol
   (c) Increased human chorionic gonadotropin
3. *Karyotyping* (more accurate diagnostic test) of the cells is done by the following procedures:
   (a) Chorionic villus sampling, done between 10 and 12 weeks of gestation
   (b) Amniocentesis (done between 16 and 20 weeks of gestation)
   (c) Percutaneous umbilical blood sampling (PUBS). Although these procedures are about 98%–99% accurate in their detection of Down's syndrome, there is an increased risk of miscarriage because these tests are performed inside the uterus. Because of this risk, they are recommended primarily for women older than 35 years. Chorionic villus sampling is usually performed between 8 and 12 weeks of pregnancy, amniocentesis between 12 and 20 weeks, and PUBS is usually performed after 20 weeks of pregnancy.
   (d) Study of foetal cells in the maternal circulation by fluorescence in situ hybridisation (FISH) technique
   (e) Foetal cord blood sampling

Karyotype shows any of the following:
- Non-disjunction (Trisomy 21)—in 95% of the cases
- Translocation—in 4% of the cases
- Mosaicism (mixture of normal cell lines with Trisomy 21)—in 1% of the cases

CAUSES OF EARLY DEATH

- Congenital heart disease
- Leukaemia
- Lower respiratory tract infections
- Atlantoaxial dislocation
- Alzheimer's disease

RECENT ADVANCES

Various studies and researches are being conducted in the children with Down's syndrome. The findings are encouraging.

The symptoms of Down's syndrome such as dry skin, sparse hair and hypotonia are also seen in amino acid, vitamin and mineral deficiencies.

Also superoxide dismutase, an antioxidant enzyme, is encoded in the lower arm of chromosome 21.

TURNER'S SYNDROME

Turner's syndrome is a chromosomal disorder that occurs in females when there is lack of one X chromosome. A normal female has 46 chromosomes, of which two are X chromosomes. In Turner's

syndrome, one of these X chromosomes is either missing or defective. Karyotyping may show any of the following findings:

- 45 XO (most common)
- Mosaics (45 XO/46XX, 45 XO/46XY)—one X chromosome is missing in some cells only
- Other mosaics with isochromosomes, rings or fragments

INCIDENCE

The incidence is estimated to be about 1 in 2000–2500 live born females. The frequency at conception is 3%, but 99% of these are spontaneously aborted. It is generally sporadic and not associated with advanced maternal age.

CLINICAL FEATURES (PHENOTYPE)

1. In newborn (Figs. 15.4–15.6)
   - Short length
   - Low birth weight
   - Low set, abnormal ears
   - Redundant skin with transverse folds at the back of the neck (webbed neck)
   - Lymphoedema of dorsum of hands and feet, which may extend to the anterior tibial region
   - Low posterior hairline
   - Gonadal dysgenesis
2. In older children
   - Short stature (the mean adult height achieved is 140 cm) (during the first 3 years the rate of growth is normal)
   - Ears having long, narrow auricles with hypoplastic helix and superior crux of antihelix
   - Ptosis of eyelids
   - High arched palate
   - Short neck, webbing of neck and low posterior hairline
   - Broad shield-like chest (with illusion of widely placed nipples)
   - Cubitus valgus (increased carrying angle at the elbow)—the angle between the arm and the forearm is widened
   - Fine and wrinkled skin in the palms
   - Hyperconvex finger nails

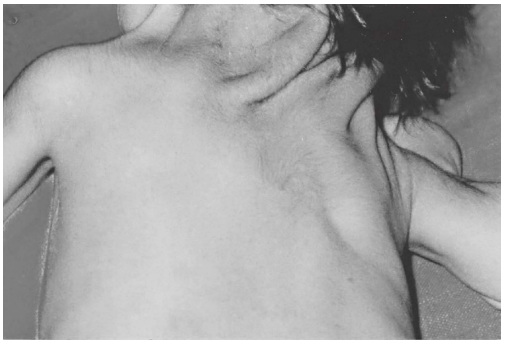


FIGURE 15.4 Webbing of neck in Turner's syndrome. Note the increased skin folds in the nape of neck



FIGURE 15.5 Bilateral pedal oedema.



FIGURE 15.6 Newborn female with Turner's syndrome. Note the webbing of neck, wide carrying angle at the elbow joint and bilateral pedal oedema.

SYSTEMWISE FINDINGS

Cardiovascular System

Congenital heart diseases such as bicuspid aortic valve (50%), coarctation of aorta, dissecting aortic aneurysm and mitral valve prolapse are the common cardiac anomalies associated with Turner's syndrome.

Hypertension is common even in the absence of cardiac or renal disease.

Kidney

- Horse shoe kidney
- Duplex ureters
- Ectopic kidney, abnormal renal vasculature with double collecting system

Reproductive System

- Sexual infantilism (infantile uterus and vagina)
- Primary amenorrhoea
- Genital hypoplasia
- Failure of development of secondary sexual characters (decreased or absent secondary sexual hair—axillary and pubic hairs)
- Delayed puberty
- Sterile

Endocrine System

- Primary hypothyroidism (10%–30%)
- Growth retardation (short stature with delayed bone age)
- Type 1 diabetes mellitus
- Obesity

Skeletal System

- Skeletal dysgenesis of knee and wrist
- Cubitus valgus (increased carrying angle at the elbow)
- Fine and wrinkled skin in the palms
- Short fourth metacarpal (brachymetacarpia)
- Scoliosis

Development

- Normal intelligence quotient; some may have subnormal intelligence
- Minor defect in spatial perception

INVESTIGATIONS

1. Karyotype—done from buccal smear (X-chromatin negative)
   - 45 XO
   - Some patients may be mosaic (have two cell lines)
   - Some patients may have both the X chromosomes, but one X chromosome may be structurally abnormal (X-chromatin negative, but may be abnormal)
2. Ultrasound abdomen and pelvis—hypoplastic uterus, poorly developed ovaries and renal malformations
3. Exploratory laparotomy—'streak' ovaries, which consists of connective tissue with few germ cells
4. Urinary and serum FSH—elevated; 17-ketosteroids will be low
5. Echocardiography—cardiac malformations
6. Thyroid profile
7. Blood sugar
8. Hearing assessment

TREATMENT

1. Medical
   - Initiation of cyclic hormone therapy by the age of 12–14 years.
   - Recombinant human growth hormone alone or in combination with an anabolic steroid.
   - Replacement therapy with oestrogen after 12 years.
2. Surgical
   - Coarctation of aorta and the webbed neck should be corrected by surgery.
3. Supportive
   - Psychosocial support should be given.

COMPLICATIONS

- Development of gonadoblastomas from the dysgenetic ovaries in patients with Y line.
- Common occurrence of sensorineural deafness.
- Recurrent otitis media.

PROGNOSIS

Most of the foetuses with Turner's syndrome are spontaneously aborted in the first trimester. It is important to recognise patients with Turner's syndrome at an early age to ensure optimal physical growth. Development of secondary sexual characteristics can be improved with hormone replacement therapy. Increase in height can be achieved with oestrogens.

Spontaneous pubertal development and menses, as a consequence of residual ovarian function, have been observed in 20%–25% and 2%–5% of patients with Turner's syndrome, respectively. Nearly 30 pregnancies in spontaneously menstruating women with Turner's syndrome have been reported. Successful pregnancies have occurred using ovum donation and in vitro fertilisation.

MALE TURNER'S SYNDROME

- Karyotyping shows 46XY.
- Lymphoedema is more common in males than in females. Pulmonary stenosis, aortic stenosis and cryptorchidism are common.
- Pulmonic stenosis is the common lesion in males with Turner's syndrome and XO/XX. Coarctation is common in cases with XO.

KLINEFELTER'S SYNDROME

Klinefelter's syndrome is the most common aneuploidy in males caused by an extra X chromosome.

INCIDENCE

The disease incidence rate has been found to be 1 in 500 newborn boys and 1% in children with mental retardation.

CHROMOSOMAL PATTERNS

Chromatin constitution is 47 XXY. Apart from 47 XXY, this syndrome can have various other chromosomal patterns:

1. Mosaic patterns
   - 46 XY/47 XXY
   - 46 XY/48 XXYY
   - 45 x/46 XY
2. 48 XXXY
3. 49 XXXXY

CLINICAL FEATURES

1. In early childhood
   - Eunuchoidal body proportions
   - Mental retardation (average IQ approximately 85–90)
   - Gynaecomastia
   - Bony deformities at the elbow leading to restricted supination and flexion
   - Tall stature (arm span generally greater than height)
   - Slim
   - Decreased weight
   - Upper segment/lower segment ratio—decreased due to long legs
   - Psychosocial problems—excessively shy or aggressive
   - Fire-setting behaviour
2. In adolescents and adults
   - Failure of development of secondary sexual characters such as facial hair
   - Gynaecomastia
   - Hypogonadism
   - Infertility
   - Lack of libido
   - Genital abnormalities—small phallus, small testes, testicular atrophy, cryptorchidism and hypospadias

INVESTIGATIONS

1. Increased gonadotropin levels—LH and FSH levels increased. LH and FSH response

to gonadotropin-releasing hormones will be elevated in older children after 12 years of age
2. Testicular biopsy—small testes with hyalinised seminiferous tubules, arrest of spermatogenesis and predominance of Sertoli cells
3. Karyotyping
4. Testosterone levels—decreased
5. Oestradiol/testosterone ratio—increased

TREATMENT

Replacement therapy with long-acting testosterone should be started by 11–12 years of age in a dose of 25–50 mg intramuscularly every 3–4 weeks. The dose should be increased by 50 mg every 6–9 months until a maintenance dose of 200–250 mg is reached.

PROGNOSIS

Mosaic pattern has a better prognosis. The severity of Klinefelter's syndrome is related to the number of X chromosomes. Mental retardation and impairment of virilisation are severe when the number of X chromosomes exceeds two.

CHAPTER 16

Muscular Disorders

HISTORY TAKING

Age

Age of onset depends on the type of disease:

- Congenital muscular dystrophy (CMD) is present at birth or infancy.
- Duchenne muscular dystrophy (DMD) occurs in children before the age of 4 years. In most cases, patients become bedridden by the age of 13 years. If they are ambulant by the age of 16 years, it is less likely to be DMD and goes more in favour of Becker dystrophy. Death occurs by 18–20 years.

Sex

DMD and Becker dystrophy occur in males.

Place

It is important to know the place to which the child belongs.

- Lathyrism causing muscle weakness is seen in some areas of Bangladesh, Nepal and India and may be misdiagnosed as a case of muscular dystrophy.
- Fukuyama type of CMD is common in Japan.

Presenting Complaints

- Weakness
- Wasting/hypertrophy of muscles (pseudohypertrophy—enlargement of calf and deltoid muscles)

History of Present Illness

Ascertain the following history to elicit the nature and severity of weakness.

- H/o weakness—upper limbs/lower limbs; proximal/distal (most of the myopathies involve the proximal muscles except myotonic dystrophy which involves the distal muscles)
- H/o progressive difficulty in walking
- H/o frequent falls
- H/o enlargement of muscles (pseudohypertrophy of calf muscles)
- H/o involuntary movements, convulsions
- H/o sensory disturbances (paraesthesia)
- H/o bladder/bowel involvement
- H/o fatigability (hyperparathyroidism is associated with muscle weakness and muscle wasting)
- H/o constipation and intolerance to cold (hypothyroidism)
- H/o weakness associated with generalised hypertrophy of muscles (Kocher–Debre–Semelaigne syndrome is associated with hypothyroidism) (see Fig. 14.6)
- History related to complications—breathlessness (cardiomyopathy, respiratory failure), musculoskeletal deformities/contracture and learning disabilities

History of Past Illness

- H/o drug intake—anabolic steroids (hypertrophy of muscles) and corticosteroid (steroid induced myopathy)
- H/o rash (myositis causing weakness of muscles)

Antenatal History

This includes the history of decreased foetal movement (hypothyroidism).

Birth History

- The baby with DMD appears normal at birth.
- Arthrogryposis (joint contractures) may be seen at birth in CMD.

Neonatal History

The baby with DMD appears normal in the newborn period, whereas CMD includes a number of autosomal recessive diseases of muscle weakness and possible joint deformities, which are present at birth and progress slowly.

Developmental History

- Motor milestones delayed—many children are not able to walk before 18 months of age. They also have difficulty in climbing the stairs.
- Head control is delayed in CMD.
- Intellectual impairment—intelligence is impaired in DMD. Mental retardation is not progressive.

Nutritional History

Malnutrition is associated with nutritional myopathy.

Immunisation History

Administration of intramuscular injections such as DPT vaccine may be associated with the inability to walk due to pain. This should not be confused with myopathies.

Personal History

A child with muscle weakness avoids outdoor activities and prefers to remain indoors.

Family History

A positive family history is present in facioscapulohumeral dystrophy (Landouzy–Dejerine disease), DMD and Becker dystrophy.

Social and Environmental History

Nutritional myopathy is common in low socioeconomic groups.

The history taking should be followed by the detailed physical examination of the child.

CLINICAL EXAMINATION

General Examination

- Neurocutaneous markers (weakness due to neuropathy)
- Features of hypothyroidism (endocrine myopathy)
- Features of malnutrition (nutritional myopathy)
- Features of Cushing's syndrome (steroid-induced myopathy)
- Rashes are common in myositis

Vital Signs

- Sleeping pulse rate—decreases in hypothyroidism (endocrine myopathy)
- Respiratory rate—increases if the vital capacity is decreased. Nocturnal hypoventilation is an early sign of impending respiratory failure
- Blood pressure—decreases in hypothyroidism (endocrine myopathy)
- Temperature—decreases in hypothyroidism (endocrine myopathy)

Anthropometry

- Weight—obesity is common in these children due to decreased energy expenditure because of decreased motor activity

- Height
- Midarm circumference

All these parameters will be decreased in severe protein energy malnutrition, which will be associated with nutritional myopathy.

Systemic Examination

Nervous System

1. Higher functions
   - Mental retardation (hypothyroidism)
   - Intellectual impairment—intelligence quotient will be about 70%
2. Cranial nerves
   - Tongue fibrillation
   - Bulbar muscle weakness
3. Motor system
   - Bulk—wasting of muscles; pseudohypertrophy (DMD) of calf muscles, gluteus, deltoid, infraspinatus, quadriceps muscles
   - Tone—flabby
   - Power (weakness)—there is weakness of pretibial muscles (foot drop) and shoulder girdle. Diaphragm and facial muscles are rarely involved
   - Reflexes—all deep tendon jerks except ankle jerks are lost early in the illness. Ankle jerks may be brisk and even clonus may be elicited
   - Gait—waddling



FIGURE 16.1 Gower's sign---the child appears to climb on himself.

   - Gower's sign—when children try to get up from the floor, they appear to climb on themselves due to proximal muscle weakness (Fig. 16.1)
4. Sensory system—sensory involvement is seen in neuropathies
5. Autonomic system—sphincters are unaffected
6. Examination of spine—exaggerated lumbar lordosis due to weakness of pelvic muscles

Cardiovascular System

Cardiomyopathy is associated with DMD.

Respiratory System

- Respiratory infections are common—respiratory and pharyngeal muscle weakness lead to frequent infections because of aspiration.
- Decreased vital capacity.
- Respiratory failure—nocturnal hypoventilation may be an early sign of impending respiratory failure in DMD.

MUSCULAR DYSTROPHIES

Muscular dystrophy is a group of hereditary muscle diseases that weaken the muscles that move the human body. It is characterised by progressive skeletal muscle weakness, defects in muscle proteins, and the death of muscle cells and tissue.

Criteria of muscular dystrophy are as follows:

- Primary myopathy
- Genetic basis
- Progressive course
- Degeneration and death of muscle fibres at some stage of disease

Common muscular dystrophies are Duchenne, Becker, limb-girdle, congenital, facioscapulohumeral, myotonic, oculopharyngeal and Emery–Dreifuss. Of these Duchenne and Becker muscular dystrophies are discussed here.

DUCHENNE MUSCULAR DYSTROPHY

It is the most common hereditary neuromuscular disorder and is inherited in an X-linked recessive

manner. Incidence is 1:3500 live born male infants. It is characterised by progressive weakness of a selective group of muscles without involvement of the nervous system.

Age of Onset

- 3–10 years
- Many children are not able to walk before 18 months of age. The clinical disability is suspected earlier with a positive family history
- The patient usually dies by the age of 18 years.

Sex

1. Males are commonly affected.
2. Symptomatic females with DMD are explained by
   (a) Turner's girls—DMD possible.
   (b) DMD possible with autosomal recessive inheritance.
   (c) Lyon hypothesis—symptomatic females are explained by the Lyon hypothesis in which the normal X chromosome becomes inactivated and the defective X chromosome is active.
   (d) Homozygous parents.
3. Affected girls show mild weakness.

Carrier State

- Eighty per cent of carriers has high serum creatinine kinase and 20% has normal serum creatinine kinase.
- Female carrier state shows no expression clinically.

Genetics

- Inheritance—X-linked inheritance.
- Abnormal gene (DMD gene) is on X chromosome at Xp21 locus.
- Duchenne DNA has only 14 Kb against 20,000 Kb.
- Deletion at the breakpoint of Xp21 in the DNA leads to little or no dystrophin (a protein of sarcolemmal membrane) in the affected child.

Molecular Genetics

It includes isolation and cloning of the Duchenne gene and the identification of dystrophin as the encoded protein that is deficient in DMD. This forms the basis for confirming the suspected cases, carrier detection, precise prenatal diagnosis and opportunity for cure by gene slicing and replacement.

Pathology

- Degenerative changes and fibrosis of muscle
- Variation of the muscle fibre diameter
- Scattered degenerating and regenerating myofibres
- Foci of mononuclear inflammatory cell infiltrates as a reaction to muscle fibre necrosis
- Endomysial connective tissue proliferation
- Mild architectural changes in still functional fibres
- Hypercontracted fibres probably result from segmental necrosis at another level, allowing calcium to enter the site of breakdown of the sarcolemmal membrane and trigger a contraction of the muscle fibre
- Type 1 fibres predominate

Clinical Features

Characteristic Features

- Pseudohypertrophy of the calf muscles and wasting of thigh muscles (Fig. 16.2)
- Intellectual impairment



FIGURE 16.2. Calf pseudohypertrophy in a case of DMD.

- Early loss of all deep tendon jerks except the ankle jerk which is present till late in the illness. It may be brisk or even show clonus
- Waddling gait
- Positive Gower's sign

Other features

- Muscles involved—proximal muscles of the upper and lower limbs are predominantly affected. Distal muscles are relatively spared so that the child is able to write and hold a cup. Respiratory and pharyngeal muscle weakness leads to recurrent infections and change in voice.
- Pseudohypertrophy of calves is followed by that of tongue and forearm muscles.
- Progressive weakness and delay in motor milestones.
- No myalgia, muscle spasm and fasciculations.
- Cardiomyopathy is a constant feature and results in congestive heart failure.
- Late events—ankle contractures (common), scoliosis, exaggerated lumbar lordosis, incontinence of anal and urethral sphincter (uncommon).

The clinical presentation depends upon the age at presentation

1. *Infancy*
   - Usually asymptomatic at birth and in early infancy.
   - Gross motor skills (rolling over, sitting, standing) are usually achieved or mildly delayed.
   - Poor head control may be the first sign of weakness.
   - No distinctive facies, but facial weakness is a late event.
   - Walking may be at 18 months; hip girdle weakness may be seen as early as second year.
2. *Childhood*
   - Lordotic posture to compensate the gluteal weakness.
   - Gower's sign is evident by 3 years and fully expressed by fifth or sixth year.
   - Trendelenberg gait or hip waddle appears later.
   - Ambulation is possible up to 12 years of age.
   - Progression continues in the second decade.
   - Airy or nasal voice.

Associated Conditions

- Macroglossia
- Skeletal deformities
- Cardiac abnormalities
- Absence of incisor teeth
- Mental retardation (attributed to the defect of dystrophin in the brain)
- Seizures are more common than in general population

Course of Disease

The clinical evolution is divided into three stages:

1. Stage of ambulation
2. Wheel chair bound stage
3. Bedridden stage

Progression continues in the second decade. In most cases, the patient becomes bedridden by the age of 13. If he/she is ambulant by the age of 16, it is less likely to be DMD and more likely to be Becker dystrophy. Death occurs by the age of 20 either due to cardiac or respiratory failure. Nocturnal hypoventilation may be an early sign. The association of mental retardation with DMD is well documented and is attributed to the defect of dystrophin in the brain.

Complications

- Acute dilatation of stomach
- Behavioural problems
- Bony deformities—scoliosis
- Contracture of muscles
- Cardiomyopathy—CCF
- Decreased vital capacity—respiratory problem
- Intellectual impairment—mental retardation
- Respiratory and pharyngeal weakness leads to frequent infections because of aspiration
- Respiratory failure
- Rhabdomyolysis during anaesthesia

Investigations

1. *Serum creatinine kinase (CK)* is greatly elevated even in presymptomatic stages. The clinical

diagnosis is confirmed by elevated CK (50–100 times more than normal values). Normal values are less than 160 U/L. In DMD, the values are elevated to 15,000–35000 U/L. Normal serum creatinine kinase is incompatible with diagnosis of DMD, although in terminal stages, the serum creatinine kinase may be low (less muscle mass to degenerate). Normally, creatinine kinase is very high for the first 3–4 days of life (newborn).

2. *Muscle biopsy*—Duchenne designed a harpoon-like biopsy needle to obtain biopsy with less pain and bleeding. While taking biopsy, the criteria given in Table 16.1 should be taken care of for selection of the site of biopsy. Deltoid, biceps, gastrocnemius and quadriceps muscles are common sites for biopsy.
   - Muscle biopsy shows dystrophic muscle changes like necrosis, fibre splitting, rounding up of small fibres, hypercontracted/opaque muscle fibres, myopathic grouping, muscle fibre degeneration and regeneration, sacrolemmal nuclear proliferation with connective tissue and adipose tissue infiltration, endomysial fibrosis.
   - Dystrophin studies in the muscle biopsy show complete absence of the protein when stained with a special dye to visualise it.
3. *Other lysosomal enzymes* such as aldolase, AST and lactate dehydrogenase are also increased but less specific.
4. *ECG, X-ray chest* are done for evaluation of cardiac involvement. ECG shows deep 'Q' wave in limb leads in cardiomyopathy.
5. *Electromyogram (EMG)* is done to confirm myopathic pattern and rule out neurogenic causes. EMG is non-specific in myopathy and there is no evidence of denervation.
6. *Nerve conduction velocity (NCV) studies*—Motor and sensory nerve conduction velocities are normal.

TABLE 16.1 Criteria for Selection of Muscles for Biopsy

Duration of Disease	Criteria for Selection
Acute cases	Muscles that are severely/moderately affected
Chronic cases	Muscles that are moderately affected and not severely affected

7. *Nerve biopsy*—whole sural nerve should be biopsied. This gives a clue to the aetiology like inflammatory, demyelinating, hereditary or systemic causes.
8. *Ultrasound/MRI scan of muscles.*
9. *Molecular genetic studies* using DNA probes are the most specific for accurate diagnosis. It can be done on a blood sample without subjecting the patient to biopsy. Currently used methods look for gene deletion, gene duplication and gene sequencing. *PCR test* to detect defect in Xp21 is diagnostic and is useful in early diagnosis, prenatal diagnosis and carrier detection. *Western blot* techniques to confirm the absence of dystrophin establishes the diagnosis.
10. Investigations for complications
    - ECG, X-ray chest—For evaluation of cardiac involvement. ECG shows deep 'Q' wave in limb leads in cardiomyopathy
    - Pulmonary function tests
    - Intelligence quotient/development quotient tests

Diagnosis

1. In a child with typical clinical features and a positive family history (where diagnosis was confirmed by muscle biopsy), only serum CK levels are required to establish the diagnosis; muscle biopsy is not required in such cases.
2. Muscle biopsy is diagnostic. Samples are commonly taken from Vastus lateralis (quadriceps femoris) followed by gastrocnemius, deltoid, biceps, etc.
3. Molecular genetic studies using DNA probes are the most specific for accurate diagnosis.
   - Identification of dystrophin as the encoded protein that is deficient in DMD is used to confirm the diagnosis, carrier detection and antenatal diagnosis.
   - Isolation and cloning of the Duchenne gene.

Treatment

There is no medical cure or method to slow down the progression. The main aim of treatment is to maintain ambulation and prevent contractures.

1. Supportive care
   - Nutritional support—this includes preservation of good nutritional status and adequate calcium intake. There is no need for vitamin supplements
   - Physiotherapy to prevent contractures. However, excessive exercise is not advised as it accelerates the degeneration process
2. Drugs—steroids alone have been shown to have some benefits in temporarily arresting the progress up to 1 year. They decrease the rate of apoptosis or programmed cell death. Prednisolone is given in dose of 0.75 mg/kg/day and may be continued until side effects supervene. Prednisone may also be used. Deflazacort causes less side effects. Intermittent therapy with steroids for 10 days in a month prevents complications due to long-term steroid intake. Avoid fluorinated steroids like dexamethasone or triamcinolone which may induce myopathy
3. Treatment of complications
   - Congestive cardiac failure—salt-restricted diet, diuretics, digoxin
   - Pulmonary infections—antibiotics
4. Recent advances in the treatment of DMD
   - Myoblast transfer—myoblast culture is injected into the dystrophic muscle. This replaces the degenerating muscle with the healthy one that has dystrophin. Prior immunosuppression is necessary. Success is yet to be established
   - Gene therapy—gene splicing and replacement. Myoblast transfer and gene therapy are still under research and are not widely available
   - Genetic counselling

Mortality

Death usually occurs by 15–20 years of age. Causes of increased mortality are as follows:

- Respiratory failure during sleep
- Congestive cardiac failure (arrhythmias)
- Pneumonias (aspiration)
- Airway obstruction
- Acute dilatation of stomach

Causes of respiratory failure:

- Respiratory infections
- Respiratory muscle weakness
- Aspiration
- Chest deformities—scoliosis reducing the vital capacity

Prevention of DMD

The disease can be diagnosed early in the gestation, and termination of pregnancy can be considered if the defect is seen in the foetus.

Detection of Carriers

1. Creatinine kinase—80% of the carriers will have elevated serum creatinine kinase whereas the remaining 20% will have normal serum creatinine kinase.
2. PCR test to detect defect in Xp21 is diagnostic and is useful in early detection of carrier females.
3. Muscle biopsy is also done to detect the carriers.

Prenatal Diagnosis

This has revolutionised the diagnosis, and now the word 'Xp21 diseases' or 'dystrophinopathies' has come to stay. DMD-like clinical presentation in some boys with intact dystrophin and normal genetic pattern has led to the recognition of other dystrophies. Prenatal diagnosis is important in the following cases:

- A mother who has already delivered a child with DMD or her brother is affected with DMD.
- A sister is a carrier or has a child with DMD.
- Any other male on maternal side with DMD.

It is done in the following ways:

- Chorionic villus biopsy—DNA analysis by southern blot or PCR by 11–14 weeks of gestation.
- Amniocentesis—determine the sex of the foetus. In males, perform DNA analysis after 15 weeks.
- CPK levels are normally high in foetus, so these levels are not used for antenatal diagnosis.
- The foetal muscle from aborted DMD can be tested by immunocytochemistry and histochemistry.

BECKER MUSCULAR DYSTROPHY

- Genetic defect is at the same locus as that of DMD.
- Xp21 gene mutation present, but the deletion of dystrophin gene is not present. Dystrophin is present up to 20% of normal levels.
- There is an affected maternal uncle who is ambulant beyond 20 years of age.
- Inheritance—X-linked recessive.
- Age of onset—after 5 years of age. Onset is found later and patients are ambulatory beyond the age of 15 years.

Clinical Features

- Same as DMD but follows a slow, protracted course
- Muscles affected—pelvic and pectoral muscles
- Pseudohypertrophy of calf muscles

Complications

- Isolated cardiomyopathy
- Cardiac arrhythmias

Investigations

- Creatinine kinase—elevated 1500–3000 U/L
- Aldolase elevated
- SGOT (aspartate amino transferase) elevated
- Electromyogram
- Muscle biopsy

Prognosis

This condition runs a benign course. Clinically, it follows a slow, protracted course. Onset is found later and disability occurs by 15–25 years of age. However, an onset in the third decade or later can also occur. The patients may be ambulant for more than 25 years after the onset of the symptoms. Death occurs in fourth or fifth decade.

Differences between Duchenne muscular dystrophy and Becker dystrophy are enlisted in Table 16.2.

TABLE 16.2 Differences between Duchenne Muscular Dystrophy and Becker Dystrophy

Features	Duchenne Muscular Dystrophy	Becker Dystrophy
Age	Early onset, 2–5 years	Late onset, 8–10 years
Incidence	More common	Less common
Progression	Rapid	Slow
Intelligence	Subnormal	Normal
Life expectancy	15–20 years	25–30 years
Cardiomyopathy	Common	Rare
Investigations		
Dystrophin levels	Markedly reduced	Reduced
Contractures	Early	No early contractures
Associated problems	Cardiomyopathy	Colour blindness
Ambulation	Till 9–11 years	Beyond 15–20 years
Prognosis	Severe; death by 16–20 years	Less severe, benign course of illness, death in the fourth or fifth decade

MYOPATHIES

Myopathy refers to disease of the muscles which results in muscular weakness.

CLASSIFICATION

1. Hereditary myopathies
   - Muscular dystrophies (Duchenne's, Becker's, facioscapularhumeral, myotonic dystrophy)
   - Congenital myopathies (central core disease, Nemaline rod disease)
   - Mitochondrial myopathies (myoclonic epilepsy with ragged red fibres (MERRF), Leigh subacute necrotising encephalopathy, Kerans–Sayre syndrome)
   - Storage myopathies (inborn errors of metabolism—glycogen storage diseases (Von Gierke's disease, Pompe's disease, Cori–Forbes disease, Anderson's disease, McArdle's disease))

- Lipid myopathies (muscle carnitine deficiency, systemic muscle carnitine deficiency)

2. Inflammatory myopathies
   - Infective (viral, bacterial, parasitic)
   - Autoimmune (polymyositis, dermatomyositis, systemic lupus erythematosus, Sjogren's disease)
3. Endocrine myopathies (pituitary, thyroid, parathyroid, adrenal)
4. Nutritional (protein energy malnutrition, vitamin E deficiency myopathy)
5. Traumatic
   - External (physical injury, toxins (alcoholic), drug (zidovudine, clofibrate) myopathy)
   - Internal (malignancy)
6. Miscellaneous (amyloidosis, benign congenital hypotonia, electrolyte disturbances (periodic paralysis), malignant hyperthermia)

Differences between myopathy and neuropathy

Features	Myopathy	Neuropathy
Muscle weakness	Proximal (exception—myotonic muscular dystrophy)	Distal (exception—juvenile SMA)
Deep tendon reflexes	Well preserved	Lost
Sensory abnormalities	Not seen	Present
EMG	Low amplitude, short duration, polyphasic with normal interference pattern	High amplitude, long duration, polyphasic motor unit potentials, with decreased interference pattern

CHAPTER 17

Neoplasms

LEUKAEMIAS

Leukaemias are the most common type of childhood cancers. These are heterogenous group of neoplasms that originate from genetically abnormal haematopoietic cells. Basically, they are malignancies of bone marrow and blood. The bone marrow normally produces three types of blood cells—white blood cells (WBCs), red blood cells and platelets. In leukaemia, the bone marrow begins to make abnormal blood cells that do not mature properly. These immature cells reproduce at an increased pace and crowd out the healthy ones, leading to the failure of the bone marrow.

CLASSIFICATION

Leukaemia is classified according to the cells involved and the state of maturity of these cells.

I. Acute
   - Lymphoblastic
   - Myeloblastic

II. Chronic
   - Lymphocytic
   - Myeloid

Most leukaemias belong to the above-mentioned varieties. Other varieties such as subleukaemic and aleukaemic leukaemia may also be seen.

Subleukaemic leukaemia consists of a few blast cells with a slight increase in the WBC count. It is characterised by the presence of abnormal WBCs in the peripheral blood; the total number of WBCs is normal or slightly increased. *Aleukaemic leukaemia* is characterised by a normal or low number of WBCs in the peripheral blood despite leukaemic changes in the bone marrow. The bone marrow examination is required to confirm its diagnosis as there are no leukaemic cells in the peripheral blood.

HISTORY TAKING

Age

- More common in the age group of 2–10 years, with a peak incidence at 4 years.

Sex

- Male preponderance; male:female = 1.5:1.

Race

- Incidence is more in Whites than in Blacks.

Complaints

- Fever
- Swelling in the neck

History of Present Illness

- Easy fatigability
- Fever
- Bleeding episodes
- Bone pain
- Purpura—bleeding in skin (thrombocytopaenia)
- Weight loss
- Pressure symptoms—chest pain, dysphagia (oesophageal obstruction), cough and dyspnoea (airway obstruction), swelling of neck and face due to obstruction of SVC, oliguria (renal obstruction)
- Pallor and pancytopenia (bone marrow involvement)
- Features suggestive of Down's syndrome (as leukaemias are more common in children with Down's syndrome)

Treatment History

- Chemotherapy for Hodgkin's disease or other cancers
- Immunosuppressive therapy
- H/o irradiation
- Drugs—chlorambucil, nitrosouria, melphalan, procarbazine

Family History

- The sibling of a person with leukaemia and the second twin of the affected twin are more prone.
- If the first twin is affected in the first year of life, the chance of the second twin getting affected is >70%.
- If the first twin is affected later than first year, the risk of the other twin getting affected is twice that in the general population.

ACUTE LYMPHOBLASTIC LEUKAEMIA

Acute lymphoblastic leukaemia (ALL) is more common in the age group of 2–15 years with a peak incidence between 2 and 4 years. It affects males more often than females (M:F::1.5:1). Whites are more commonly affected than Blacks.

Classification

Morphological Classification

French–American–British (FAB) Classification. The malignant cells in the bone marrow are classified into the following types on the basis of cell size, nucleocytoplasmic ratio, nuclear shape, number of nucleoli, etc. (Table 17.1).

- ALL-L1: Small round blast cells with scanty cytoplasm (small uniform cells—good prognosis), most common
- ALL-L2: Large, heterogenous cells with variable cytoplasm (large varied cells)
- ALL-L3: Large, homogenous cells with abundant cytoplasm (large uniform cells with vacuoles—bad prognosis)

Classification Based on Immunophenotype

On the basis of surface markers present on the abnormal lymphoblastic cells, most cases of ALL can be classified into the following:

- B-cell precursor ALL (85%)—early pre-B and pre-B

TABLE 17.1 FAB Classification of ALL

Morphological Features	Subtypes		
	L1	L2	L3
Cell size	Small, homogenous	Large, heterogenous	Large, homogenous
Cytoplasm	Scanty	Variable	Moderately abundant
Cytoplasmic basophils	Slight	Slight intense	Prominent
Vacuole count	Variable	Variable	Numerous
Nucleoli	Small and inconspicuous, indistinct or not viable	Large, one or more per cell	Prominent, large
Nuclear shape	Regular, occasional clefts	Irregular clefting and indentation	Regular, oval to round
Nuclear chromatin	Fine or clumped	Fine	Fine

- B-cell ALL (1%)
- T-cell ALL (15%)

A few cases have biphenotypic leukaemia (both myeloid and lymphoid derivation).

Classification Based on Cytogenetics

It is based on the abnormalities in chromosome number and structure.

- Hyperdiploidy—Chromosome number is more than 50. It carries good prognosis.
- Hypoploidy—Chromosome number is less than 45.
- Pseudodiploidy—Normal chromosomal number with abnormalities such as translocations. It carries poor prognosis. For instance, translocation t(9;22), also known as Philadelphia chromosome, carries worst prognosis.
- Near haploidy—Chromosome number approximately equals the number of haploid cells in most of the blast cells. Some cells may show hyperdiploidy. It carries worst prognosis.

Predisposing Conditions

Some of the factors which may predispose children to leukaemias are as follows:

- Environmental factors—radiation, herbicides, pesticides, maternal use of alcohol, chronic exposure to benzene and exposure to alklyating agents.
- Viral infections—herpes, HIV, human lymphotrophic virus and Epstein–Barr virus (EBV).
- Immunodeficiency syndromes—Wiscott–Aldrich syndrome, congenital hypogammaglobulinaemia and ataxia telangiectasia.
- Genetic disorders—Trisomy 21 and Patau's syndrome (Trisomy 13), Bloom's syndrome and Fanconi's anaemia.
- Drugs—chlorambucil, nitrosourea, melphalan and procarbazine.
- Family history—the sibling of a person with leukaemia and the second twin of the affected twin are more prone. If the first twin is affected in the first year of life, the chance of the second twin getting affected is greater than 70%. If the first twin is affected later, the risk for the second twin will be twice as that in general population.
- Second malignancy due to treatment with antimalignant drugs such as alklyating agents.

Clinical Features

- Easy fatigability and pallor (anaemia)
- Fever due to infections of skin, urinary tract and lungs (infection due to granulocytopaenia)
- Bleeding episodes, purpura and petechiae (thrombocytopenia)
- Bone pain and tenderness (bone marrow infiltration and expansion due to increased activity)
- Respiratory distress and pleural effusion
- Hepatosplenomegaly
- Lymphadenopathy
- CNS involvement—meningeal irritation, cranial nerve palsy, diencephalic syndrome (voracious appetite, obesity and hemiplegia)
- Testicular enlargement—firm and painless (infiltration)
- Other features depending on the organ infiltrated (e.g. heart, ovaries and skin).

Investigations

- Haemogram—anaemia
- Total count increased
- Differential count—lymphocyte count increased; blast cells will be present
- Platelet count—decreased
- Increased serum levels of uric acid, potassium, phosphorus, calcium and lactate dehydrogenase (LDH)
- Blood smear—blast cells
- Chest X-ray—mediastinal mass
- Bone marrow examination for cytology, cytochemistry, blast immunology, chromosomal analysis, DNA content, etc. Marrow is hypercellular and shows >25% lymphoblasts.
- Lumbar puncture—increased cell count

Treatment

The cornerstone of treatment is a combination chemotherapy for the control of the active disease together with CNS prophylaxis for the prevention of CNS relapses. The step-wise approach for the treatment of ALL consists of the following:

1. Chemotherapy
2. CNS prophylaxis
3. Supportive therapy
4. Treatment of relapse

Chemotherapy

Induction of Remission (4–6 Weeks). Remission is defined as the absence of blast cells in the peripheral smear and the presence of less than 5% blast cells in the marrow. It is usually achieved within 4–5 weeks with the therapy given in the induction phase.

The aim of the induction of remission is to eradicate leukaemic cells and preserve the normal bone marrow. This includes the following:

1. Systemic therapy
   - Vincristine 1.5 mg/m^2/week IV (maximum 2 mg)
   - Prednisolone 40 mg/kg/m^2/day orally (maximum 60 mg)
2. Intrathecal treatment (triple therapy)
   - Methotrexate 15 mg/m^2 (maximum 15 mg)
   - Hydrocortisone 15 mg/m^2 (maximum 15 mg)
   - Cytosine arabinoside 30 mg/m^2 (maximum 30 mg)

These are given weekly for 6 weeks during induction and then every 8 weeks for 2 years.

Remission Maintenance (2–3 Years). The maintenance therapy is given for 2–3 years to prevent relapses. It consists of systemic continuation of the following drugs:

- 6-Mercaptopurine 50 mg/m^2/day orally
- Methotrexate 20 mg/m^2/week orally

Intermittent doses of vincristine and prednisolone may be given if required.

CNS Prophylaxis

It is given to eradicate the leukaemic cells that have crossed the blood–brain barrier. It is usually given in the form of radiation and/or intrathecal therapy.

Supportive Therapy

- Blood transfusion
- Antibiotics for infection
- Adequate hydration to be maintained to avoid renal toxicity due to drugs

Treatment of Relapse

Bone marrow relapse is common. Treatment consists of the following:

- Marrow ablative chemotherapy followed by allogenic transplantation of stem cells for early bone marrow relapse.
- Intensive chemotherapy for late bone marrow relapse.

Complications of Treatment

- Secondary malignancy
- Endocrine dysfunction
- Cardiomyopathy
- Neurophysiological changes

Prognosis

Mortality is seen in 60% of cases. Prognosis depends on various factors, as given in Table 17.2.

ACUTE MYELOID LEUKAEMIA

It is also known as *acute myelogenous leukaemia* (AML). It is a malignancy of the myeloid line of blood cells, characterised by the rapid growth of abnormal WBCs that accumulate in the bone marrow. Differentiating features between ALL and AML are given in Table 17.3.

Predisposing Factors

1. Chromosomal disorders
   - Trisomy 21
   - Bloom's syndrome
   - Fanconi's anaemia
   - Diamond Blackfan anaemia
   - Kostmann's syndrome
   - Shwachman–Diamond syndrome
   - Li-Frauemeni syndrome
   - Neurofibromatosis type I
2. Drugs
   - Alkylating agents
   - Topoisomerase inhibitors
   - Epipodophyllotoxins
3. Ionising radiation

TABLE 17.2 Prognostic Factors for ALL

Features	Good Prognostic Factors	Bad Prognostic Indicators
Age at presentation	2–10 years	<2 and >10 years
Sex	Female	Male
Race	Black	White
Examination		
CNS involvement at diagnosis	Absent	Present
Lymphadenopathy	Absent	Present
Hepatosplenomegaly	Absent, <3 cm	Present, >3 cm
Mediastinal mass	Absent	Present
Extramedullary secondaries	Not present	Present at diagnosis
CNS secondaries	Absent	Present
Investigations		
Anaemia	Absent (Hb >10 g%)	Present (Hb <10 g%)
RBC count	Normal	Decreased
WBC count at diagnosis	<10,000/mm^3	>50,000/mm^3
Radiological findings	No mediastinal widening	Mediastinal widening
Platelet count	>1,00,000 cells/mm^3	<20,000 cells/mm^3
LDH	Not high	High
Lymphoblasts	L1	L2 or L3
PAS stain	Positive	Negative
Immunoglobulins	Normal IgA, IgG, IgM	Decreased IgA, IgG, IgM
Mitotic and labelling index	Low	High
Cell type	Non-T, non-B, B-cell precursor ALL	T or B cells Mature B cell ALL with t(8;14), t(9;22) or t(4;11)
Glucocorticoid receptors	High number	Low number
Chromosomal studies	Hyperdiploidy (as the number of chromosomes increase the prognosis will be good)	Pseudodiploidy with normal number of chromosomes
Response to induction	L1 or L2 marrow <5% blasts on day 14	L3 marrow >25% blasts on day 14, persistence of extramedullary disease
Remission	Early (<4 weeks)	Late (>4 weeks)

TABLE 17.3 Differences between ALL and AML

Features	ALL	AML
Incidence	Commonest malignancy in children	15%–20% of childhood leukaemia
Age	Younger age	Adolescence
Progress	Rapid	Slow progress
Clinical features		
Chloroma (collection of leukaemic cells)	–	+
Blue berry muffin lesions	–	+
Infiltration of gingiva	–	+
Bulk disease	Lymphadenopathy, massive hepatosplenomegaly common	Not common
CNS symptoms	Less common	More common
DIC	Not common	Common in acute promyelocytic leukaemia M_3
Investigations		
Nuclear/cytoplasmic ratio	High	Low
Stain for myeloperoxidase	–	+
Sudan black stain	–	+
TdT (terminal deoxynucleotidyl transferase) cell surface marker	+	–
Treatment	Chemotherapy	Aggressive chemotherapy
Prognosis	Good, 70% cure rate	Low remission rate, only 40% cure rate, increased relapse

Classification

According to the FAB classification, AML is classified into the following types:

- M0—minimally differentiated acute myeloblastic leukaemia.
- M1—acute myeloblastic leukaemia, without maturation.

- M2—acute myeloblastic leukaemia, with granulocytic maturation.
- M3—promyelocytic or acute promyelocytic leukaemia (APL).
- M4—acute myelomonocytic leukaemia.
- M4eo—myelomonocytic together with bone marrow eosinophilia.
- M5—acute monoblastic leukaemia (M5a) and acute monocytic leukaemia (M5b).
- M6—acute erythroid leukaemias, including erythroleukaemia (M6a) and very rare pure erythroid leukaemia (M6b).
- M7—acute megakaryoblastic leukaemia.

Clinical Features

All the findings that are present in ALL in association with bone marrow failure may also be seen in cases of AML. CNS symptoms are more common in AML than in ALL. The clinical features of AML include the following:

- Fever
- Anaemia and pallor (infiltration of the bone marrow)
- Hepatosplenomegaly
- Bleeding
- Disseminated intravascular coagulation (DIC) (in promyelocytic leukaemia)
- Chloromas (granulocytic sarcomas) are seen in the CNS, bones, orbit and epidural spaces in M2 subtype
- Blueberry muffin lesions (subcutaneous nodules)
- Infiltration of gingiva and gum hypertrophy
- Leukaemia cutis (AML-M4 and AML-M5)

Investigations

To Diagnose AML

1. Complete blood count
   - Abnormal WBCs (leucocytosis)
   - Decrease in platelets and red blood cells
   - Rarely low WBC count (leucopenia)
2. Bone marrow cytology
   - Morphology—the bone marrow is hypercellular and shows the monotonous pattern of myeloid monocyte megakaryocytic series
   - Cytochemistry—it is positive for Sudan black and myeloperoxidase.

To Find Out the Subtype

- Flow cytometry for identification of cell surface antigens
- Cytogenetic studies

These investigations help in deciding the type of treatment required.

Treatment

It consists of aggressive chemotherapy (for induction and consolidation) and bone marrow transplantation in addition to supportive therapy.

Induction of remission is usually achieved by the use of cytosine arabinoside and doxorubicin. Relapse rate is high without further therapy. Consolidation therapy or post-remission therapy is usually done with cytosine arabinoside and etoposide. M3 patients are treated with retinoic acid, in addition to chemotherapy. Allogenic bone marrow transplantation can be done after achievement of remission.

Complications

- Bleeding
- DIC in promyelocytic leukaemia
- Severe myelosuppression following treatment
- High mortality rate due to infection and bleeding

Prognosis

With aggressive chemotherapy, remission can be achieved in about 80% of patients.

CHRONIC MYELOID LEUKAEMIA

Chronic myeloid leukaemia (CML) is of two main types—juvenile and adult variety.

Juvenile CML

Juvenile chronic myeloid leukaemia (JCML) is a rare chronic myeloproliferative disorder. Cell stem origin evidence exists for leukaemic involvement of

CD34-positive stem cells and monocytes. It occurs in infancy and early childhood, usually before 5 years, and is not associated with Philadelphia chromosome, which is characteristic of CML.

Clinical Features

It has a rapid fatal course. Clinical features are non-specific, for example:

- Fever
- Malaise
- Weight loss
- Lymphadenopathy
- Anaemia
- Hepatosplenomegaly
- Infection
- Thrombocytopenia
- Skin involvement (eczema, xanthoma)

Investigations

- Leucocytosis and monocytosis
- Thrombocytopenia
- Anaemia
- Myelodysplastic pattern in bone marrow

Treatment

- Supportive therapy
- Allogenic stem cell transplant

Adult Variety of CML

Adult variety of CML (ACML) is the classic form of CML. It occurs in children older than 5 years. It is commonly associated with Philadelphia chromosome (Ph) translocation 22 and 9. ACML has two phases in the natural course of illness—chronic phase followed by accelerated or 'blast-crisis' phase after 3–4 years of onset.

Clinical Features

Patients are often asymptomatic at diagnosis, presenting incidentally with an elevated WBC count on a routine laboratory test. Few of them may present with fever, malaise, weight loss, etc. Other clinical features are as follows:

- Massive splenomegaly
- Lymphadenopathy
- Hepatomegaly
- Mild anaemia
- Thrombocytosis

Investigations

- Anaemia
- Leucocytosis
- Decreased leucocyte alkaline phosphatase

Treatment

- During chronic phase, chemotherapy is given with busulfan or hydroxyurea. Recently, α-interferon and imatinib mesylate have also been used.
- Allogenic stem cell transplantation (Table 17.4).

TABLE 17.4 Differences between Treatment of Acute and Chronic Leukaemia

Features of Treatment	Acute Leukaemia	Chronic Myeloid Leukaemia
Aim	To eradicate the leukaemic cells	To control the disease
Dose	High dose, aggressive chemotherapy	Low-dose chemotherapy

Prognosis

The patient survives for only a few months after blast transformation takes place. Bad prognostic indicators are very high leucocyte count and presence of more than 5% blast cells in the marrow at the time of diagnosis.

CONGENITAL LEUKAEMIA

Congenital myeloblastic leukaemia is more common than congenital lymphoblastic leukaemia. It usually presents in the first month of life. Proliferation of immature leukaemic cells and infiltration to the non-haemopoietic tissues are usually seen.

Criteria for diagnosis of congenital leukaemia are as follows:

- Proliferation of immature haemopoietic tissues.
- Infiltration of the immature cells into non-haemopoietic tissues.
- Absence of other disease processes such as infections and haemolytic disorders.

Predisposing Conditions

- Down's syndrome
- Turner's syndrome
- Mosaic monosomy
- Klinefelter's syndrome
- Trisomy 13
- Bloom's syndrome
- Mosaic trisomy
- Trisomy D and E

Clinical Features

- Leukaemia cutis (skin lesions)—it consists of non-tender multiple nodules that are easily moveable over the subcutaneous tissue. Leukaemic infiltration of skin is common in preterm
- Petechiae and ecchymosis
- Hepatosplenomegaly
- Respiratory distress (due to lung infiltration)

Investigations

- Complete blood count—anaemia and thrombocytopenia
- Peripheral blood smear for cellular morphology to identify the type of leukaemic cells

Treatment

It is the same as for AML.

Differences between congenital leukaemia and leukaemias of childhood are summarised in Table 17.5.

TABLE 17.5 Differences between Congenital Leukaemia and Leukaemias of Childhood

Features	Congenital Leukaemia	Leukaemias of Childhood
Common type	Myeloblast	Lymphoblast
Anaemia	Not common	Common
Skin infiltration	Common	Not common

LYMPHOMAS

The term *lymphoma* refers to malignant proliferation of the lymphoreticular system. Lymphatic tissues include the lymph nodes, thymus, spleen, tonsils, adenoids and bone marrow, as well as lymphatics or lymph vessels. Although many types of cancer eventually spread to the lymphatic system, lymphomas are distinct because they actually originate there. The incidence of lymphoma increases with age. Lymphomas are of two types—*Hodgkin's lymphoma* (HL) and *non-Hodgkin's lymphoma.* Together, they are the third most common type of malignancy in children.

HISTORY TAKING

Age

- Bimodal incidence

Sex

- Common in males.

Complaints

- Fever—periodic fever associated with HL is known as Pel–Ebstein fever
- Painless, swollen lymph nodes in the neck, chest, underarms or groin
- Night sweats
- Itchy skin

History of Present Illness

- Dry cough
- Recurrent fever > 38.3°C
- Weight loss (>10% in 6 months)
- Night sweats
- Generalised pruritis
- Pressure symptoms—chest pain, oesophageal obstruction (dysphagia), airway obstruction (cough, dyspnoea), swelling of neck and face due to obstruction to SVC, etc.
- Increasing pallor (pancytopenia)
- CNS involvement—cranial nerve palsy
- Unexplained pain on taking alcohol
- H/o loss of appetite

History of Past Illness

- H/o pre-existing immunodeficiency disorders.
- H/o HIV infection (AIDS), EBV, cytomegalovirus (CMV), human herpes virus 6 etc.

Treatment History

- Immunosuppressive therapy
- Irradiation

Family History

Clustering of cases is seen in families. There may be a genetic predisposition. The risk increases about 100-fold in an unaffected monozygotic twin. The risk is not increased in a dizygotic twin.

CLINICAL EXAMINATION

General Examination

- Pallor due to anaemia (bone marrow involvement)
- Fever—Pel–Ebstein type
- Lymphadenopathy—non-tender and rubbery (cervical or supraclavicular region)

Anthropometry

During examination, it is found that the weight is decreased. The child suffers from weight loss.

Examination of Abdomen

- Hepatosplenomegaly
- Rapidly enlarging abdominal mass which may be massive in size
- Ascites

HODGKIN'S LYMPHOMA

Hodgkin's lymphoma, also known as Hodgkin's disease, is characterised by the presence of specific malignant cells, called Reed–Sternberg cells, in the lymph nodes or in some other lymphatic tissue. *Reed–Sternberg cells* are large malignant lymphoid cells of B-cell origin, 15–45 µm in diameter with multiple or multilobulated nuclei. They are surrounded by reactive normal T cells, plasma cells and eosinophils. Males are more commonly affected. It is rare in children younger than 10 years. Incidence is bimodal with regard to age; first peak is at 15–35 years and the second peak is seen above 50 years of age.

Aetiology

The aetiology is not known but increased incidence is seen following infection with EBV, CMV and human herpes virus 6. Hodgkin's disease has a genetic predisposition as it is common in members of the same family and in certain races. Immunological disorders (such as systemic lupus erythematosus [SLE], ataxia telangiectasia, AIDS, rheumatoid arthritis) are associated with an increased risk for the disease.

Classification

On the basis of number of Reed–Sternberg cells and the surrounding reactive cells, Hodgkin's disease is classified as follows:

I. Rye classification

1. Lymphocyte predominant
2. Nodular sclerosing
3. Mixed cellularity
4. Lymphocyte-depleted

II. New WHO/Revised European–American Lymphoma (REAL) classification of lymphoid neoplasms

1. Nodular lymphocyte predominance
2. Classical Hodgkin's lymphoma
3. Lymphocyte predominant
4. Nodular sclerosing
5. Mixed cellularity
6. Lymphocyte-depleted
7. Anaplastic large-cell lymphoma (ALCL) Hodgkin like

Clinical Features

1. Lymphadenopathy (painless, non-tender, firm and rubbery) is commonly seen in cervical or supraclavicular region; may be present in mediastinal, axillary and inguinal region
2. Constitutional symptoms
   - Fever, weight loss, night sweats and pruritis
   - Hepatosplenomegaly
   - Symptoms due to airway compression by enlarged nodes—dyspnoea and wheeze
   - Unexplained pain on taking alcohol
   - Anaemia
   - Leucopaenia in advanced cases; infection due to T-cell dysfunction

Differential Diagnosis

- Infectious mononucleosis
- Toxoplasmosis
- Atypical tuberculosis
- Non-Hodgkin's lymphoma (lymphocyte predominant)

Investigations

- Haemogram—anaemia, neutropenia, thrombocytopenia
- ESR—increased
- LDH—raised (a poor prognostic indicator)
- X-ray chest—shows mediastinal widening due to enlargement of mediastinal nodes
- CT scan—chest and abdomen
- MRI scan—chest and abdomen
- Lymph node biopsy—Reed–Sternberg cells

Treatment

Appropriate therapy is selected on the basis of staging of Hodgkin's disease.

Staging of Hodgkin's Disease

According to the Ann-Arbor classification there are four stages of Hodgkin's disease—I, II, III and IV. Suffixes E, S or ES are used according to the involvement of extralymphatic site, spleen or both (Table 17.6). All cases are further classified as A or B according to the presence or absence of constitutional symptoms. Suffix A is used when there are no systemic symptoms and it carries good prognosis. Suffix B is used when any of the constitutional features such as unexplained or recurrent fever above 38.3°C for three consecutive days, weight loss (>10% in the last 6 months) or night sweats are present. It carries poor prognosis (Table 17.7).

TABLE 17.6 Ann-Arbor Classification of Hodgkin's Lymphoma

Stages	Features
I	Involvement of a single lymph node region (I) or an extra lymphatic site (IE)
II	Involvement of two or more lymph node regions (II) or an extra lymphatic site or lymph node regions on one side of the diaphragm (IIE)
III	Involvement of lymph node regions on both sides of the diaphragm without extra lymphatic involvement (III) or with extra lymphatic involvement (IIIE). The spleen may be involved (IIIS). The combination of both of the above may occur (IIISE)
IV	Diffuse involvement of one or more extralymphatic tissues (liver and bone marrow)

Radiotherapy

Indications

- Stage I disease
- Stage II disease with three or few areas involved
- After chemotherapy
- Sites with pressure symptoms

Complications

- Growth retardation
- Impaired organ function—heart, ovary, thyroid, etc.
- Second malignancy

Chemotherapy

Indications

- All patients with B symptoms
- Stage II disease with more than one area involved
- Stage III and IV diseases

Drugs

- Chlorambucil—6 mg/m^2 (up to 10 mg total)
- Vinblastine—6 mg/m^2 (up to 10 mg total)
- Procarbazine—100 mg/m^2
- Prednisolone—40 mg/ m^2
- Cyclophosphamide—650 mg/m^2 (IV)
- Adriamycin—25 mg/m^2 (IV)

TABLE 17.7 Further Classification of Hodgkin's Lymphoma

Constitutional Features	Classification	
	A	B
Fever	Absent	Present
Weight loss	Absent	Present
Night sweats	Absent	Present
Prognosis	Good	Worst

- Etoposide—100 mg/m² (IV)
- Vincristine—0.4–1.4 mg/m² (up to 2 mg) (IV)
- Bleomycin—10 mg/m² (IV)
- Dacarbazine—375 mg/m² (IV)

Combination Chemotherapy Regimens

- MOPP (mechlorethamine [nitrogen mustard], vincristine, prednisolone and procarbazine)
- COPP (cyclophosphamide, vincristine [oncovin], prednisolone and procarbazine)
- ABVD (Adriamycin [doxorubicin], bleomycin, vinblastine and dacarbazine)
- BEACOPP (bleomycin, etoposide, Adriamycin [doxorubicin], cyclophosphamide, vincristine [oncovin], procarbazine and prednisone)

Complications

- Myelodysplasia
- Acute leukaemia
- Azoospermia
- Second malignancy

Prognosis

Prognosis is poor in the presence of following factors:

- Presence of B symptoms
- Bulk disease—size of mediastinal mass is more than one-third of the chest diameter; nodal aggregate >10 cm
- Hilar adenopathy
- Nodal involvement at more than three sites
- Extensive splenic involvement
- Stage IV Hodgkin's disease
- Mixed cellularity or lymphocyte-depleted histologies

NON-HODGKIN'S LYMPHOMA

Non-Hodgkin's lymphoma (NHL) results from the malignant growth of B or T cells in the lymphatic system. In children and adolescents, most NHLs are high-grade diffuse tumours with clinically aggressive behaviour. These are rapidly growing tumours. At the time of presentation, the disease is usually advanced with the involvement of bone marrow and CNS.

Predisposing Factors

1. DNA repair immunodeficiency syndromes
   - Severe combined immunodeficiency
   - Wiskott–Aldrich syndrome
   - X-linked lymphoproliferative disorder
2. Genetic disorders
   - Bloom's syndrome
   - Ataxia telangiectasia
3. Acquired immunological disorders
   - Viral infections—human immunodeficiency virus (AIDS) and EBV
   - Following immunosuppressive therapy

Classification

Most of the childhood NHLs can be classified into the following types (Table 17.8):

I. Lymphoblastic lymphomas (LBL)—30%
II. Small non-cleaved cell lymphoma (SNCL)—40%

TABLE 17.8 REAL Classification of Non-Hodgkin's Lymphoma

Types	Precursor Cells	Clinical Features/Site of Involvement
Lymphoblastic lymphomas	Precursor T cells (80%) Precursor B cells (20%)	Presents as lymphadenopathy (cervical, axillary or mediastinal mass) Rapidly spreads to brain, bone marrow, lungs, heart and other lymph nodes
Small, non-cleaved types	Undifferentiated B cell derived—Burkitt's and non-Burkitt's	Tends to develop in facial bones or abdomen as localised tumours of bowel wall or diffuse abdominal disease; rapidly spreads to brain
Large-cell lymphomas	Large-cell B Large-cell T	Intermediate grade malignancy, tends to develop in the neck, chest (mediastinum, thymus), throat or abdomen and often spreads quickly to the skin. This type rarely spreads to the bone marrow or brain.

1. Burkitt's lymphoma
2. Non-Burkitt's lymphoma

III. Large-cell lymphomas (LCL)—30%

1. Large cell (B cells)
2. Immunoblastic lymphoma (ILCL)—B cells
3. ALCL—T cells

Cytogenetics

Some of the pathological subtypes are associated with cytogenetic aberrations:

- Burkitt's lymphoma is associated with translocation between chromosomes 8 and 14, that is, t(8;14) or t(2;8) or t(8;22).
- ALCL is associated with t(2;5).
- DLBCLs and LCLs are associated with a variety of cytogenetic abnormalities.

Clinical Features

The clinical features depend on the pathological subtype (Table 17.8), primary site of involvement (extranodal sites—mediastinum, abdomen, head and neck), staging of the disease (Table 17.9) and secondary site of involvement (bone marrow, central nervous system). The following clinical features are usually seen:

- Night sweats
- Fever with chills
- Itching
- Lymphadenopathy usually painless, rapid lymph node enlargement—causes pressure symptoms at the primary site (Table 17.10)
- Loss of weight and appetite

TABLE 17.9 St. Jude Staging System for Childhood NHL

Stage	Features
I	Single tumour (single nodal or extranodal) excluding mediastinum and abdomen
II	Single tumour (extranodal) with regional node involvement Two or more nodal areas on the same side of the diaphragm Two extranodal tumours with or without regional node involvement on the same side of diaphragm Primary gastrointestinal tumour in the iliocaecal area with or without involvement of mesenteric nodes
III	All primary intrathoracic tumours Two extranodal sites on both sides of the diaphragm Two or more nodal areas on both sides of the diaphragm Extensive intra-abdominal tumours
IV	Any of the above with CNS or bone marrow involvement

TABLE 17.10 Pressure Symptoms on the Basis of Site of Involvement

Site involved	Pressure Symptoms
Thorax	Chest pain, dyspnoea
Airway obstruction	Cough, dyspnoea
GIT	Dysphagia, intestinal obstruction
Superior vena cava	Swelling of neck, face
Spinal cord	Acute paraplegia
Cranial nerves	Cranial nerve palsy

Secondary sites are involved in stages III and IV. Common secondary sites involved are gastrointestinal system (dysphagia), bone marrow (pancytopenia) and CNS (cranial nerve palsy).

Investigations

- Complete blood count
- Serum electrolytes, uric acid, lactate dehydrogenase, creatinine, calcium and phosphorus
- Liver function tests
- CSF cytology (pleocytosis), cell count and proteins
- Abdominal ultrasonography
- X-ray chest
- CT scan—neck, chest, abdomen and pelvis
- Lymph node biopsy—histology and immunophenotypelogy
- Bone marrow biopsy

Treatment

- Radiotherapy—rarely used in cases of NHL.
- Systemic chemotherapy—different combination chemotherapy regimens such as COMP (cyclophosphamide, vincristine, prednisolone, methotrexate) are used.
- If the cells in the marrow exceed 25%, the condition should be treated as ALL (Table 17.11).

TABLE 17.11 Treatment of Non-Hodgkin's Lymphoma

Type	Subtype	Treatment
Lymphoblastic lymphomas	Precursor T Precursor B	ALL treatment
Small, non-cleaved types	Burkitt's and non-Burkitt's	Chemotherapy
Large-cell lymphomas	Large-cell B	Chemotherapy
	Large-cell T	ALL treatment

- Recurrent NHL can be treated with bone marrow transplantation.

Complications

- Superior vena cava syndrome
- Acute paraplegia (secondary to compression of spinal cord or central nervous system)
- Tumour lysis syndrome
- Metabolic abnormalities—hyperuricaemia, hyperphosphataemia, hyperkalaemia and hypocalcaemia

Prognosis

Pregnosis is good in localised B-cell type lymphoma.

Differences between Hodgkin's and non-Hodgkin's lymphoma

Features	Hodgkin's lymphoma	Non-Hodgkin's lymphoma
Age	Bimodal incidence (20–30 years and >50 years)	All ages; risk increases with increasing age
Sex	Males > Females 3–7 years—M:F–4:1 7–9 years—M:F–3:1 >10 years—1.3:1	M:F—3:1
Predisposing factors	Immunodeficiency Epstein–Barr virus	Chemotherapy Immunodeficiency
Affected organs	Lymph nodes Liver Spleen Bone marrow Lungs	Mediastinum Abdomen Head and neck CNS Bone marrow
Pathology	Reed–Sternberg cell	Involves T- or B-cells
Progression	Depends on the type	High-grade malignancy; rapidly growing tumours
Clinical features	Progressive weakness Loss of weight Night sweats Pruritis Lymphadenopathy (cervical, mediastinal, axillary, inguinal)	Lymphadenopathy (painless) Lassitude Fever Sweating Splenomegaly Extralymphatic symptoms depend upon type of NHL CNS involvement—Cord compression Bone marrow involvement—pain Pressure symptoms—dysphagia
Extra nodal involvement	Less common	More common
Prognosis	Better if treated early	Bad

Appendix

TABLE A.1 Length/height and weight percentiles for girls and boys aged 0–60 months

Month	GIRLS						BOYS					
	Length/height (cm)			Weight (kg)			Length/height (cm)			Weight (kg)		
	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th
0	45.6	49.1	52.7	2.4	3.2	4.2	46.3	49.9	53.4	2.5	3.3	4.3
1	50.0	53.7	57.4	3.2	4.2	5.4	51.1	54.7	58.4	3.4	4.5	5.7
2	53.2	57.1	60.9	4.0	5.1	6.5	54.7	58.4	62.2	4.4	5.6	7.0
3	55.8	59.8	63.8	4.6	5.8	7.4	57.6	61.4	65.3	5.1	6.4	7.9
4	58.0	62.1	66.2	5.1	6.4	8.1	60.0	63.9	67.8	5.6	7.0	8.6
5	59.9	64.0	68.2	5.5	6.9	8.7	61.9	65.9	69.9	6.1	7.5	9.2
6	61.5	65.7	70.0	5.8	7.3	9.2	63.6	67.6	71.6	6.4	7.9	9.7
7	62.9	67.3	71.6	6.1	7.6	9.6	65.1	69.2	73.2	6.7	8.3	10.2
8	64.3	68.7	73.2	6.3	7.9	10.0	66.5	70.6	74.7	7.0	8.6	10.5
9	65.6	70.1	74.7	6.6	8.2	10.4	67.7	72.0	76.2	7.2	8.9	10.9
10	66.8	71.5	76.1	6.8	8.5	10.7	69.0	73.3	77.6	7.5	9.2	11.2
11	68.0	72.8	77.5	7.0	8.7	11.0	70.2	74.5	78.9	7.7	9.4	11.5
12	69.2	74.0	78.9	7.1	8.9	11.3	71.3	75.7	80.2	7.8	9.6	11.8
13	70.3	75.2	80.2	7.3	9.2	11.6	72.4	76.9	81.5	8.0	9.9	12.1
14	71.3	76.4	81.4	7.5	9.4	11.9	73.4	78.0	82.7	8.2	10.1	12.4
15	72.4	77.5	82.7	7.7	9.6	12.2	74.4	79.1	83.9	8.4	10.3	12.7
16	73.3	78.6	83.9	7.8	9.8	12.5	75.4	80.2	85.1	8.5	10.5	12.9
17	74.3	79.7	85.0	8.0	10.0	12.7	76.3	81.2	86.2	8.7	10.7	13.2
18	75.2	80.7	86.2	8.2	10.2	13.0	77.2	82.3	87.3	8.9	10.9	13.5
19	76.2	81.7	87.3	8.3	10.4	13.3	78.1	83.2	88.4	9.0	11.1	13.7
20	77.0	82.7	88.4	8.5	10.6	13.5	78.9	84.2	89.5	9.2	11.3	14.0
21	77.9	83.7	89.4	8.7	10.9	13.8	79.7	85.1	90.5	9.3	11.5	14.3
22	78.7	84.6	90.5	8.8	11.1	14.1	80.5	86.0	91.6	9.5	11.8	14.5
23	79.6	85.5	91.5	9.0	11.3	14.3	81.3	86.9	92.6	9.7	12.0	14.8
24	80.3	86.4	92.5	9.2	11.5	14.6	82.1	87.8	93.6	9.8	12.2	15.1
25	80.4	86.6	92.8	9.3	11.7	14.9	82.1	88.0	93.8	10.0	12.4	15.3
26	81.2	87.4	93.7	9.5	11.9	15.2	82.8	88.8	94.8	10.1	12.5	15.6

(Table continued)

TABLE A.1 *(Continued)*

Month	GIRLS						BOYS					
	Length/height (cm)			Weight (kg)			Length/height (cm)			Weight (kg)		
	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th
27	81.9	88.3	94.6	9.6	12.1	15.4	83.5	89.6	95.7	10.2	12.7	15.9
28	82.6	89.1	95.6	9.8	12.3	15.7	84.2	90.4	96.6	10.4	12.9	16.1
29	83.4	89.9	96.4	10.0	12.5	16.0	84.9	91.2	97.5	10.5	13.1	16.4
30	84.0	90.7	97.3	10.1	12.7	16.2	85.5	91.9	98.3	10.7	13.3	16.6
31	84.7	91.4	98.2	10.3	12.9	16.5	86.2	92.7	99.2	10.8	13.5	16.9
32	85.4	92.2	99.0	10.4	13.1	16.8	86.8	93.4	100.0	10.9	13.7	17.1
33	86.0	92.9	99.8	10.5	13.3	17.0	87.4	94.1	100.8	11.1	13.8	17.3
34	86.7	93.6	100.6	10.7	13.5	17.3	88.0	94.8	101.5	11.2	14.0	17.6
35	87.3	94.4	101.4	10.8	13.7	17.6	88.5	95.4	102.3	11.3	14.2	17.8
36	87.9	95.1	102.2	11.0	13.9	17.8	89.1	96.1	103.1	11.4	14.3	18.0
37	88.5	95.7	103.0	11.1	14.0	18.1	89.7	96.7	103.8	11.6	14.5	18.3
38	89.1	96.4	103.7	11.2	14.2	18.4	90.2	97.4	104.5	11.7	14.7	18.5
39	89.7	97.1	104.5	11.4	14.4	18.6	90.8	98.0	105.2	11.8	14.8	18.7
40	90.3	97.7	105.2	11.5	14.6	18.9	91.3	98.6	105.9	11.9	15.0	19.0
41	90.8	98.4	106.0	11.6	14.8	19.2	91.9	99.2	106.6	12.1	15.2	19.2
42	91.4	99.0	106.7	11.8	15.0	19.5	92.4	99.9	107.3	12.2	15.3	19.4
43	92.0	99.7	107.4	11.9	15.2	19.7	92.9	100.4	108.0	12.3	15.5	19.7
44	92.5	100.3	108.1	12.0	15.3	20.0	93.4	101.0	108.6	12.4	15.7	19.9
45	93.0	100.9	108.8	12.1	15.5	20.3	93.9	101.6	109.3	12.5	15.8	20.1
46	93.6	101.5	109.5	12.3	15.7	20.6	94.4	102.2	109.9	12.7	16.0	20.4
47	94.1	102.1	110.2	12.4	15.9	20.8	94.9	102.8	110.6	12.8	16.2	20.6
48	94.6	102.7	110.8	12.5	16.1	21.1	95.4	103.3	111.2	12.9	16.3	20.9
49	95.1	103.3	111.5	12.6	16.3	21.4	95.9	103.9	111.8	13.0	16.5	21.1
50	95.7	103.9	112.1	12.8	16.4	21.7	96.4	104.4	112.5	13.1	16.7	21.3
51	96.2	104.5	112.8	12.9	16.6	22.0	96.9	105.0	113.1	13.3	16.8	21.6
52	96.7	105.0	113.4	13.0	16.8	22.2	97.4	105.6	113.7	13.4	17.0	21.8
53	97.2	105.6	114.1	13.1	17.0	22.5	97.9	106.1	114.3	13.5	17.2	22.1
54	97.6	106.2	114.7	13.2	17.2	22.8	98.4	106.7	115.0	13.6	17.3	22.3
55	98.1	106.7	115.3	13.4	17.3	23.1	98.8	107.2	115.6	13.7	17.5	22.5
56	98.6	107.3	116.0	13.5	17.5	23.3	99.3	107.8	116.2	13.8	17.7	22.8
57	99.1	107.8	116.6	13.6	17.7	23.6	99.8	108.3	116.8	13.9	17.8	23.0
58	99.6	108.4	117.2	13.7	17.9	23.9	100.3	108.9	117.4	14.1	18.0	23.3
59	100.0	108.9	117.8	13.8	18.0	24.2	100.8	109.4	118.1	14.2	18.2	23.5
60	100.5	109.4	118.4	14.0	18.2	24.4	101.2	110.0	118.7	14.3	18.3	23.8

Source: WHO (available at http://www.who.int/childgrowth/standards/en/).

TABLE A.2 Height and weight percentiles for girls and boys aged 5–10 years

Year: Month	GIRLS						BOYS					
	Height (cm)			Weight (kg)			Height (cm)			Weight (kg)		
	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th
5:1	100.6	109.6	118.6	14.2	18.3	24.3	101.6	110.3	118.9	14.6	18.5	23.8
5:2	101.1	110.1	119.2	14.3	18.4	24.6	102.1	110.8	119.5	14.7	18.7	24.0
5:3	101.5	110.6	119.7	14.4	18.6	24.9	102.6	111.3	120.1	14.8	18.9	24.3
5:4	102.0	111.2	120.3	14.5	18.8	25.1	103.1	111.9	120.7	15.0	19.0	24.5
5:5	102.4	111.7	120.9	14.7	19.0	25.4	103.5	112.4	121.3	15.1	19.2	24.8
5:6	102.9	112.2	121.5	14.8	19.1	25.7	104.0	112.9	121.8	15.3	19.4	25.1
5:7	103.3	112.7	122.0	14.9	19.3	25.9	104.4	113.4	122.4	15.4	19.6	25.3
5:8	103.8	113.2	122.6	15.0	19.5	26.2	104.9	113.9	123.0	15.5	19.8	25.6
5:9	104.2	113.7	123.1	15.2	19.6	26.5	105.4	114.5	123.5	15.7	19.9	25.8
5:10	104.6	114.2	123.7	15.3	19.8	26.7	105.8	115.0	124.1	15.8	20.1	26.1
5:11	105.1	114.6	124.2	15.4	20.0	27.0	106.2	115.5	124.7	16.0	20.3	26.4
6:0	105.5	115.1	124.8	15.5	20.2	27.3	106.7	116.0	125.2	16.1	20.5	26.7
6:1	105.9	115.6	125.3	15.6	20.3	27.5	107.1	116.4	125.8	16.3	20.7	26.9
6:2	106.3	116.1	125.8	15.8	20.5	27.8	107.6	116.9	126.3	16.4	20.9	27.2
6:3	106.8	116.6	126.4	15.9	20.7	28.1	108.0	117.4	126.9	16.5	21.1	27.5
6:4	107.2	117.0	126.9	16.0	20.9	28.4	108.4	117.9	127.4	16.7	21.3	27.8
6:5	107.6	117.5	127.4	16.1	21.0	28.7	108.8	118.4	127.9	16.8	21.5	28.1
6:6	108.0	118.0	127.9	16.3	21.2	28.9	109.3	118.9	128.5	17.0	21.7	28.3
6:7	108.4	118.4	128.5	16.4	21.4	29.2	109.7	119.4	129.0	17.2	21.9	28.6
6:8	108.9	118.9	129.0	16.5	21.6	29.5	110.1	119.8	129.5	17.3	22.1	28.9
6:9	109.3	119.4	129.5	16.6	21.8	29.8	110.5	120.3	130.1	17.5	22.3	29.2
6:10	109.7	119.9	130.0	16.8	22.0	30.1	111.0	120.8	130.6	17.6	22.5	29.5
6:11	110.1	120.3	130.6	16.9	22.2	30.4	111.4	121.3	131.1	17.8	22.7	29.8
7:0	110.5	120.8	131.1	17.0	22.4	30.8	111.8	121.7	131.7	17.9	22.9	30.1
7:1	110.9	121.3	131.6	17.2	22.6	31.1	112.2	122.2	132.2	18.1	23.1	30.4
7:2	111.4	121.8	132.1	17.3	22.8	31.4	112.6	122.7	132.7	18.2	23.3	30.7
7:3	111.8	122.2	132.7	17.5	23.0	31.7	113.0	123.1	133.3	18.4	23.5	31.1
7:4	112.2	122.7	133.2	17.6	23.2	32.2	113.4	123.6	133.8	18.5	23.7	31.4
7:5	112.6	123.2	133.7	17.8	23.4	32.4	113.8	124.1	134.3	18.7	23.9	31.7
7:6	113.1	123.7	134.3	17.9	23.6	32.8	114.3	124.5	134.8	18.8	24.1	32.0

(Table continued)

TABLE A.2 *(Continued)*

Year: Month	GIRLS						BOYS					
	Height (cm)			Weight (kg)			Height (cm)			Weight (kg)		
	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th	3rd	50th	97th
7:7	113.5	124.1	134.8	18.1	23.9	33.1	114.7	125.0	135.3	19.0	24.3	32.3
7:8	113.9	124.6	135.3	18.2	24.1	33.5	115.1	125.5	135.9	19.1	24.6	32.7
7:9	114.4	125.1	135.9	18.4	24.3	33.8	115.5	125.9	136.4	19.3	24.8	33.0
7:10	114.8	125.6	136.4	18.6	24.5	34.2	115.9	126.4	136.9	19.5	25.0	33.3
7:11	115.2	126.1	136.9	18.7	24.8	34.6	116.2	126.8	137.4	19.6	25.2	33.7
8:0	115.7	126.6	137.5	18.9	25.0	34.9	116.6	127.3	137.9	19.8	25.4	34.0
8:1	116.1	127.0	138.0	19.1	25.3	35.3	117.0	127.7	138.4	19.9	25.6	34.4
8:2	116.5	127.5	138.5	19.2	25.5	35.7	117.4	128.2	138.9	20.1	25.9	34.7
8:3	117.0	128.0	139.1	19.4	25.8	36.1	117.8	128.6	139.4	20.2	26.1	35.1
8:4	117.4	128.5	139.6	19.6	26.0	36.5	118.2	129.0	139.9	20.4	26.3	35.5
8:5	117.9	129.0	140.2	19.8	26.3	36.9	118.6	129.5	140.4	20.5	26.5	35.8
8:6	118.3	129.5	140.7	20.0	26.6	37.4	119.0	129.9	140.9	20.7	26.7	36.2
8:7	118.7	130.0	141.2	20.1	26.8	37.8	119.3	130.4	141.4	20.8	27.0	36.6
8:8	119.2	130.5	141.8	20.3	27.1	38.2	119.7	130.8	141.9	21.0	27.2	37.0
8:9	119.6	131.0	142.3	20.5	27.4	38.6	120.1	131.3	142.4	21.1	27.4	37.4
8:10	120.1	131.5	142.9	20.7	27.6	39.1	120.5	131.7	142.9	21.3	27.6	37.8
8:11	120.5	132.0	143.4	20.9	27.9	39.5	120.9	132.1	143.4	21.4	27.9	38.2
9:0	121.0	132.5	144.0	21.1	28.2	40.0	121.3	132.6	143.9	21.6	28.1	38.6
9:1	121.5	133.0	144.5	21.3	28.5	40.4	121.6	133.0	144.4	21.8	28.3	39.0
9:2	121.9	133.5	145.1	21.5	28.8	40.9	122.0	133.4	144.9	21.9	28.6	39.4
9:3	122.4	134.0	145.6	21.7	29.1	41.3	122.4	133.9	145.4	22.1	28.8	39.8
9:4	122.8	134.5	146.2	21.9	29.4	41.8	122.8	134.3	145.8	22.2	29.1	40.3
9:5	123.3	135.0	146.8	22.1	29.7	42.3	123.2	134.7	146.3	22.4	29.3	40.7
9:6	123.8	135.5	147.3	22.3	30.0	42.7	123.5	135.2	146.8	22.6	29.6	41.1
9:7	124.2	136.1	147.9	22.6	30.3	43.2	123.9	135.6	147.3	22.7	29.8	41.6
9:8	124.7	136.6	148.4	22.8	30.6	43.7	124.3	136.1	147.8	22.9	30.1	42.0
9:9	125.2	137.1	149.0	23.0	30.9	44.2	124.7	136.5	148.3	23.1	30.4	42.5
9:10	125.7	137.6	149.5	23.2	31.2	44.7	125.0	136.9	148.8	23.2	30.6	43.0
9:11	126.1	138.1	150.1	23.4	31.5	45.2	125.4	137.3	149.3	23.4	30.9	43.5
10:0	126.6	138.6	150.7	23.7	31.9	45.7	125.8	137.8	149.8	23.6	31.2	43.9

Source: WHO (available at http://www.who.int/childgrowth/standards/en/).

TABLE A.3 Head circumference percentiles for girls and boys aged 0–60 months

Month	GIRLS			BOYS		
	3rd percentile	50th centile	97th centile	3rd percentile	50th centile	97th centile
0	31.7	33.9	36.1	32.1	34.5	36.9
1	34.3	36.5	38.8	35.1	37.3	39.5
2	36.0	38.3	40.5	36.9	39.1	41.3
3	37.2	39.5	41.9	38.3	40.5	42.7
4	38.2	40.6	43.0	39.4	41.6	43.9
5	39.0	41.5	43.9	40.3	42.6	44.8
6	39.7	42.2	44.6	41.0	43.3	45.6
7	40.4	42.8	45.3	41.7	44.0	46.3
8	40.9	43.4	45.9	42.2	44.5	46.9
9	41.3	43.8	46.3	42.6	45.0	47.4
10	41.7	44.2	46.8	43.0	45.4	47.8
11	42.0	44.6	47.1	43.4	45.8	48.2
12	42.3	44.9	47.5	43.6	46.1	48.5
13	42.6	45.2	47.7	43.9	46.3	48.8
14	42.9	45.4	48.0	44.1	46.6	49.0
15	43.1	45.7	48.2	44.3	46.8	49.3
16	43.3	45.9	48.5	44.5	47.0	49.5
17	43.5	46.1	48.7	44.7	47.2	49.7
18	43.6	46.2	48.8	44.9	47.4	49.9
19	43.8	46.4	49.0	45.0	47.5	50.0
20	44.0	46.6	49.2	45.2	47.7	50.2
21	44.1	46.7	49.4	45.3	47.8	50.4
22	44.3	46.9	49.5	45.4	48.0	50.5
23	44.4	47.0	49.7	45.6	48.1	50.7
24	44.6	47.2	49.8	45.7	48.3	50.8
25	44.7	47.3	49.9	45.8	48.4	50.9
26	44.8	47.5	50.1	45.9	48.5	51.1
27	44.9	47.6	50.2	46.0	48.6	51.2
28	45.1	47.7	50.3	46.1	48.7	51.3
29	45.2	47.8	50.5	46.2	48.8	51.4
30	45.3	47.9	50.6	46.3	48.9	51.5
31	45.4	48.0	50.7	46.4	49.0	51.6

(Table continued)

TABLE A.3 *(Continued)*

Month	GIRLS			BOYS		
	3rd percentile	50th centile	97th centile	3rd percentile	50th centile	97th centile
32	45.5	48.1	50.8	46.5	49.1	51.7
33	45.6	48.2	50.9	46.6	49.2	51.8
34	45.7	48.3	51.0	46.6	49.3	51.9
35	45.8	48.4	51.1	46.7	49.4	52.0
36	45.9	48.5	51.2	46.8	49.5	52.1
37	45.9	48.6	51.3	46.9	49.5	52.2
38	46.0	48.7	51.3	46.9	49.6	52.3
39	46.1	48.7	51.4	47.0	49.7	52.4
40	46.2	48.8	51.5	47.0	49.7	52.4
41	46.2	48.9	51.6	47.1	49.8	52.5
42	46.3	49.0	51.6	47.2	49.9	52.6
43	46.4	49.0	51.7	47.2	49.9	52.7
44	46.4	49.1	51.8	47.3	50.0	52.7
45	46.5	49.2	51.8	47.3	50.1	52.8
46	46.5	49.2	51.9	47.4	50.1	52.8
47	46.6	49.3	51.9	47.4	50.2	52.9
48	46.7	49.3	52.0	47.5	50.2	53.0
49	46.7	49.4	52.1	47.5	50.3	53.0
50	46.8	49.4	52.1	47.5	50.3	53.1
51	46.8	49.5	52.2	47.6	50.4	53.1
52	46.9	49.5	52.2	47.6	50.4	53.2
53	46.9	49.6	52.3	47.7	50.4	53.2
54	47.0	49.6	52.3	47.7	50.5	53.3
55	47.0	49.7	52.4	47.7	50.5	53.3
56	47.1	49.7	52.4	47.8	50.6	53.4
57	47.1	49.8	52.5	47.8	50.6	53.4
58	47.2	49.8	52.5	47.9	50.7	53.5
59	47.2	49.9	52.6	47.9	50.7	53.5
60	47.2	49.9	52.6	47.9	50.7	53.5

Source: WHO (available at http://www.who.int/childgrowth/standards/en/).

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